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AMERICAN JOURNAL OF
DISEASES of CHILDREN

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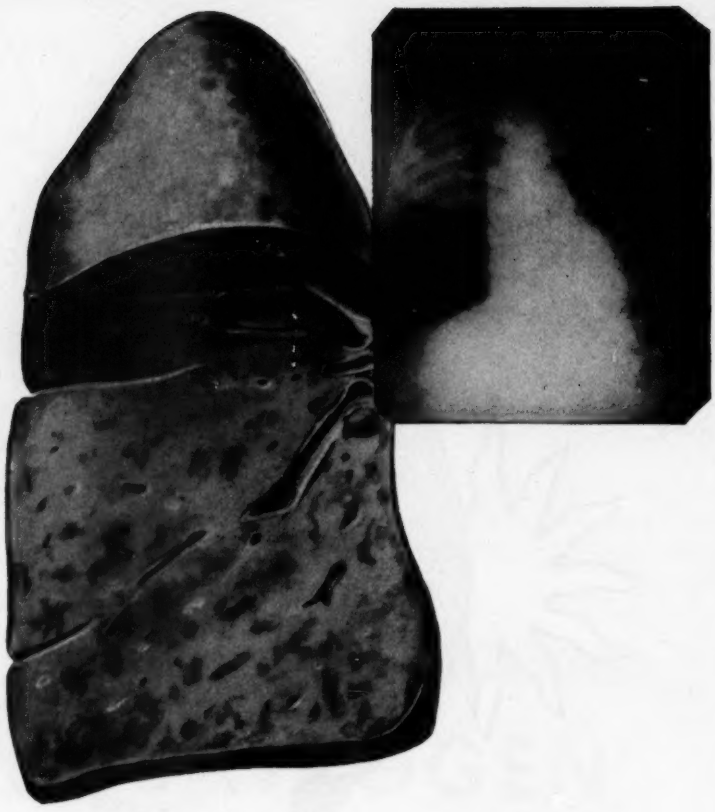

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Potterfield, T. G., and Starkweather, G. A.: J. Philadelphia General Hosp. 2:6 (Jan.) 1951

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*Watt, B.K., and Merrill, A.L.: Composition of Foods—Raw, Processed, Prepared, Agriculture Handbook No. 8, United States Department of Agriculture, Bureau of Human Nutrition and Home Economics, 1950.

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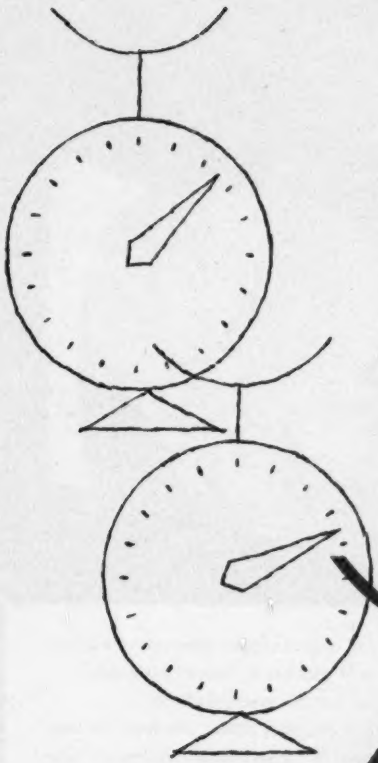

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1 Gardner, L. I., Butler, A. M., et al.: Pediatrics 5:228, 1950
2 Nesbit, H. T.: Texas State J. M. 38:551, 1943
3 Bull. National Research Council No. 119 Jan. 1950
4 Recommended Daily Dietary Allowances, Revised 1948, Food and Nutrition Board, National Research Council

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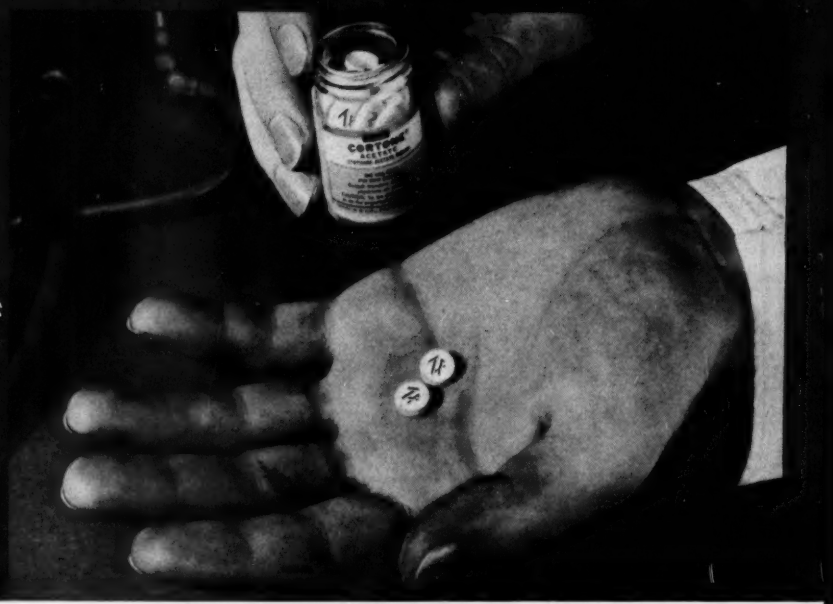

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NORCROSS, B. M., *N. Y. State J. Med.* 51: 2356, Oct. 15, 1951.

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REFERENCES

1. J.Pediatrics, 15:157
2. Am.J.Pub.Health, 37:1113

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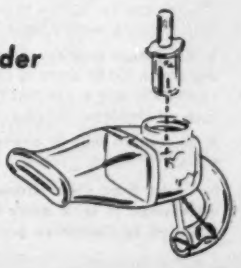

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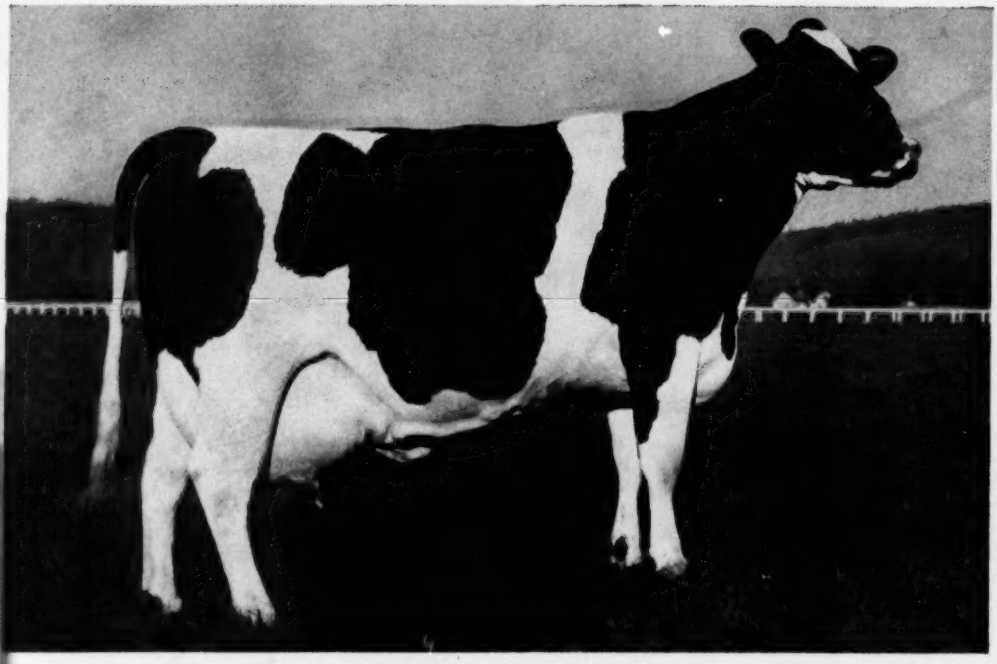

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VOLUME 83 FEBRUARY 1952 NUMBER 2

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DIFFERENTIAL DIAGNOSIS OF OLIGOPHRENIA

ROBERT GIBSON, M.D., D.P.M.
ST. ANDREWS, SCOTLAND

IN THE diagnosis of mental deficiency, dependent as it is not only on medical and psychological criteria but also on social standards, the defect must be distinguished from a considerable number of other conditions. These may conveniently be classified under the headings of intellectual defects of a less ominous nature, specific defects of a visual, auditory, or speech nature, and behavior defects in which the aberrant conduct is likely to be confused with mental defect. The following arrangement may serve to indicate the extent of these conditions:

I. Intellectual defects
- A. Educational defectiveness
- B. Dullness
- C. Backwardness

II. Specific defects
- A. Visual defects
  1. Blindness
  2. Visual cerebral injury
  3. Congenital word blindness
- B. Auditory defects
  1. Deaf-mutism
  2. High-tone deafness
  3. Congenital word deafness
- C. Speech defects
  1. Mutism
  2. Delayed development of speech
  3. Congenital motor aphasia

III. Behavior defects
- A. Delinquency
  1. Maladjustment
  2. Adolescent instability
  3. Psychopathy
- B. Convulsive defects
  1. Epilepsy
  2. Brain tumor
  3. Convulsive tic
- C. Psychoses
  1. Schizophrenias
  2. Heller's syndrome
  3. Juvenile general paralysis

In the first group, the educationally defective children are those aments within the moron range whose social development, however, is sufficiently advanced to give rise to the hope that they will not require care, supervision, and control, and who therefore can be dealt with outside the Mental Deficiency Acts.

More numerous are the children considered merely dull, probably not less than 8% of the school population. Of less general inferiority, dull children have an I. Q. of 70 to 85 on the Terman-Merrill scale.

The third variety is comprised of backward children, those whose educational attainments have fallen below the level of their natural ability, which is generally within the average range. Multiple in its origins, the causes of backwardness include such widely differing conditions as crossed laterality, mathematical disability, and environmental deprivation.[1]

Lecturer in Mental Deficiency, Division of Medicine, University of St. Andrews.

1. Burt, C. L.: The Backward Child, Ed. 3, London, University of London Press, Ltd., 1950.

The specific defects which must be differentiated from mental defect concern vision, hearing, and speech.

Among visual conditions, the exclusion of oligophrenia in cases of blindness may be possible only after prolonged observation and a careful scrutiny of the developmental history. A similar difficulty may also be experienced in visual cerebral injury, with its impaired macular vision.[2]

In congenital word blindness, on the other hand, the normal developmental history prior to schooling enables amentia to be more easily excluded, while in less pronounced cases the characteristic reversals provide a further clue.

Of the auditory group, the loss of environmental stimulation is apparent in the deaf-mute, who may indeed show some symptomatic retardation. Likelier to be overlooked is the condition of high-tone deafness, in which the effects of selective and often unsuspected deafness are to be seen in impaired attention, speech defect, and faulty spelling. In the severest cases speech is quite unintelligible, resembling the idioglossia of congenital word deafness. Congenital word deafness, with its characteristic idioglossia, well-developed mimicry, and exaggerated gestures, presents a suggestive picture; however, amentia can be excluded by the developmental history and valid performance tests.[3]

Apart from the absence of speech which is a symptom of deaf-mutism or of psychosis, mutism may occur per se as elective mutism, or as hysterical mutism, particularly in susceptible children whose parents have too soon resorted to coercive measures to force the child to talk. In this condition not only is there a complete absence of every phonated word and sound, but also the child makes absolutely no effort to speak.[4]

Delayed onset of speech, on the other hand, may be essentially a hereditary condition, in which case there is generally available a family history to show that the father or grandfather did not talk until perhaps the age of 4 years or even later. In congenital motor aphasia the child is unable to articulate clearly, and even when he is able to form isolated consonants, he cannot join them to form words. Unlike children with word deafness, these children are said to be able to recognize their errors in articulation.[5]

Behavior disorders requiring consideration can conveniently be grouped under delinquent, convulsive, and psychotic headings.

Delinquent conduct leading to the suspicion of mental defect may occur in maladjusted children, unstable adolescents, and psychopaths. Maladjustment not uncommonly leads to aggressive acts against the community, and the truancy, theft, or actual assault committed by such children often require examination to exclude mental defect. This must also be excluded in cases of instability occurring during adolescence and resulting in lying, thieving, or sexual offenses. The inability to

2. Gesell, A., and Amatruda, C. S.: Developmental Diagnosis: Normal and Abnormal Child Development, Clinical Methods and Pediatric Applications, ed. 2, New York, Paul B. Hoeber, Inc., 1947.

3. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1944.

4. Schumacher, H. C.: Nerv. Child **5**:235 (July) 1946.

5. Orton, S. T.: Reading, Writing and Speech Problems in Children: A Presentation of Certain Types of Disorders in the Development of the Language Faculty, New York, W. W. Norton & Company, Inc., 1937.

control emotions, the lack of responsibility, and the absence of prudence which are so often shown are highly reminiscent of oligophrenic behavior patterns. Confusion is even likelier in the case of psychopaths, in whom antisocial behavior is associated with grave personality disorder resulting in outstanding selfishness, marked callousness, and total absence of shame.

The question of mental defect is likely to arise in cases of epilepsy, brain tumor, and convulsive tic. In epilepsy the true level of intelligence may be masked as the result of fits or owing to the drug used, and failure to make allowance for this can result in a false diagnosis of oligophrenia. Apart from idiopathic epilepsy, fits may also occur in cerebral tumor, and when this is associated with deterioration in conduct and intellect, the resulting picture may closely resemble mental defect. The third condition under this heading is that variously known as convulsive tic, multiple tic, maladie des tics, or Gilles de la Tourette's disease. As tics are of very frequent occurrence in low-grade defectives, it is hardly surprising that such a diagnosis should be entertained in convulsive tic, with its widespread involuntary movements, its inarticulate cries, and its coprolalia.[6]

In the third group are the psychoses, with the bizarre and unpredictable behavior which often may well be mistaken for oligophrenia. The conditions included here are the schizophrenias, Heller's syndrome of infantile dementia, and juvenile general paralysis. Schizophrenic illness may appear as early infantile autism, as childhood schizophrenia, or later in adolescence as the adult type. In early infantile autism the true state of affairs is suggested by the limitation of speech, stereotypy of behavior, and indifference to surroundings, all in such contrast to the alert, intelligent expression, the beatific smile, and the quick, well-coordinated movements. Also likely to be confused is childhood schizophrenia, with its reduction of activities and falling-off in school work and standards, its excessive daydreaming, and its unmotivated impulsiveness. The later variant which is likely to cause difficulty is the simple-hebephrenic type.[7]

In Heller's syndrome of infantile dementia, shown by Corberi to be associated with a diffuse lipid degeneration of ganglion cells, there is, after a few years of normal development, a rapid loss of speech, replaced ultimately by inarticulate grunting. Together with this is a loss of comprehension and a state characterized by tic-like movements, gesturing, grimacing, and bizarre overactivity. Finally, consideration should be given to juvenile general paralysis, which, when of the simple dementing type, may closely simulate oligophrenia.

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6. Mahler, M. S., and Rangell, L.: Psychiatric Quart. **17**:579 (Oct.) 1943.
7. Kanner, L.: Child Psychiatry, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1949.

PHYSIOLOGICAL KNOCK-KNEE

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IN THE course of routine pediatric practice, many physiological phenomena are observed that seem to be common knowledge but are actually poorly recorded. An example is the presence of knock-knees between the ages of 1 and 6 years. I was unable to find any definite discussion of this in several textbooks of pediatrics [1] or in a survey of the literature.

Because of the ever increasing practice of preventive medicine, these minor points become more important, in the instance of knock-knee for several reasons: First, the practitioner should know that "knock-knee" is normal and to what degree he may consider it to be physiological. Second, there should be a fairly accurate

Knock-Knee in Children

Age, Yr.	Number of Children	Range, Cm.	Average, Cm.
1	32	0-1.5	0.25
1-2	27	0-3.0	1.5
2-3	51	0-3.5	1.9
3-4	40	0-2.0	1.1
4-5	55	0-2.0	0.95
5-6	34	0-1.5	0.5

technique of measuring the distance between the medial malleoli in order that one can determine the need for treatment of pathological knock-knee. If some therapy is indicated, then comparative figures would give the physician an index as to the success of his treatment. Third, many shoe clerks are calling attention to this condition, and the parents are beginning to ask their doctor whether or not a special corrective shoe is necessary.

A reasonably accurate measurement may be obtained with the patient lying on his back. The knees are held together firmly with one hand while the distance between the medial malleoli is measured with the other hand. The feet should be held at 90 degrees, since a lesser or greater angle will change the distance between the medial malleoli.

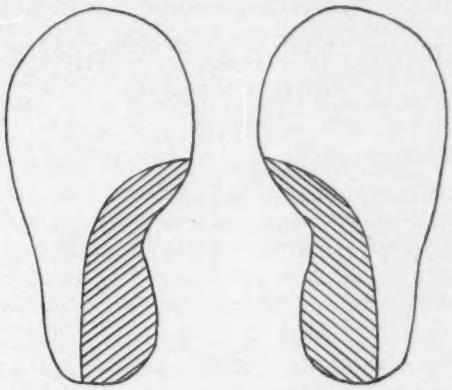
An attempt was made to establish normal figures for each year by measuring children in the office and in nursery schools. Two hundred thirty-nine children

1. Grulee, C. G., and Eley, R. C.: The Child in Health and Disease: A Textbook for Students and Practitioners of Medicine, Baltimore, Williams & Wilkins Company, 1948. Nelson, W. E., editor: Mitchell-Nelson Textbook of Pediatrics, ed. 5, Philadelphia, W. B. Saunders Company, 1950. McQuarrie, I., editor: Brennemann's Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1948.

were used in the study. The results are shown in the table. There was so little difference between boys and girls that the data are not given separately.

Seven children were omitted from the above figures because it was felt that their measurements exceeded the average so much that they were definitely pathological.

It is obvious from the table that the child at 3 years has the greatest deviation, and it is now felt that a distance of over 3.5 cm. at this age is evidence that a special shoe is indicated.



Position of wedge to be added to inner border of the shoe.

A simple corrective treatment is that of adding a wedge on the inner border of the shoe.[2] This varies from 1/8 to 3/16 of an inch (0.32 to 0.48 cm.), depending upon the amount of correction needed. The figure shows the position of the wedge.

SUMMARY

A simple method for measuring the amount of knock-knee is described. Average figures are given for children between 1 and 6 years of age.

2. Whitman, R.: A Treatise on Orthopaedic Surgery, Ed. 9, Philadelphia, Lea & Febiger, 1930, p. 648.

CHRONIC PANNICULITIS WITH LEUCOPENIA (WEBER-CHRISTIAN SYNDROME)

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CHRONIC panniculitis with leucopenia (Weber-Christian syndrome) is characterized by recurrent crops of subcutaneous nodules which occur during febrile periods and shows on histological examination a particular kind of fat atrophy. Weber [1] described this in 1925, giving it the name of "relapsing nonsuppurative nodular panniculitis." He considered this disease as similar to those described by Pfeifer [2] in 1892 and Gilchrist and Ketron [3] in 1916. Later, in 1928, Christian [4] added the word "febrile" to Weber's original title. Since that time the term Weber-Christian disease, or occasionally syndrome, has been used to describe the condition. Few cases have been reported as acute or chronic panniculitis.

Fifty-six cases similar to that originally described by Weber have been reported since that time. Our reason for reporting the present case is that, in a review of the literature on chronic panniculitis of the Weber-Christian type, this is the second recorded instance in which the etiological agent proved to be bacterial. The case is also of the youngest child, aged 8½ months, to be reported in the American and English literature.

REPORT OF A CASE

History and Physical Examination.—G. W., an 8½-month-old white boy, was first seen at the Presbyterian Hospital, Chicago, on April 9, 1951, with the presenting complaints of "skin eruption and intermittent fever" of two and one-half months' duration.

The parents stated that their baby was apparently healthy until two and a half months before, when they noticed a dusky-red lesion about the size of a quarter on the lower abdomen. Similar areas appeared later in other body regions in the following order: flank, chest, back, neck, chin, thighs, and legs. At the same time the child became irritable when moved and had an

From the Department of Pediatrics of the Presbyterian Hospital and of the University of Illinois.

1. Weber, F. P.: Relapsing Non-Suppurative Nodular Panniculitis, Showing Phagocytosis of Subcutaneous Fat Cells by Macrophages, Brit. J. Dermat. **37**:301 (July) 1925.

2. Pfeifer, V.: Über einen Fall von herdweiser Atrophie des subcutanen Fettgewebes, Deutsches Arch. klin. Med. **50**:438, 1892.

3. Gilchrist, T. C., and Ketron, L. W.: A Unique Case of Atrophy of the Fatty Layer of Skin, Preceded by the Ingestion of the Fat by Large Phagocytic Cells: Macrophages, Bull. Johns Hopkins Hosp. **26**:291 (Oct.) 1916.

4. Christian, H. A.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Arch. Int. Med. **42**:338 (Sept.) 1928.

intermittent fever, the temperature being between 100 and 100.2 F. at all times. At no time did any of these involved areas break down.

The baby was hospitalized by one of us (F. S.) at the Englewood Hospital, where results of throat culture, blood culture, routine blood work, and roentgenograms were normal. He was given penicillin for 11 days, followed by sulfadiazine and chloramphenicol (chloromycetin®). His condition did not improve, and he was discharged. After a few days at home, he was admitted to Michael Reese Hospital, where a biopsy specimen of the subcutaneous tissue and skin from the left flank was taken. The baby was again given penicillin. The pathologist, Dr. Otto Saphir, reported microscopic changes compatible with a diagnosis of Weber-Christian disease.

The child then was taken home and was later admitted to the Presbyterian Hospital. The past history was essentially normal. The birth weight was 8 lb. 9 oz. (3,884 gm.), and the weight gain had been normal. There was no history of previous illness or of contagion.

His admittance weight was 26 lb. (11,793 gm.), and he was both acutely and chronically ill, with a temperature of 101 F., lethargy, and extreme irritability on any movement. There were multiple indurated, irregular lesions which varied in color from pale red to dark purple. Induration was more marked in the center with central involution. These lesions were nontender, showed no increased warmth, and ranged in size from 0.5 to 10.0 cm. Areas involved were the anterior part of the neck and chin, bilaterally the outer margins of the face and jaws, the upper chest, the lower back, both upper thighs, the elbows, and the ankles. Other positive physical findings included a soft Grade I apical systolic murmur, enlargement of the liver to 4 cm. below the costal margin, and edema of the right lower extremity, which was thought due to a large area of induration present.

Results of Laboratory Examinations.—Blood examination showed 9 gm. of hemoglobin, 3,540,000 red blood cells, and 3,300 white blood cells with 70 to 80% polymorphonuclear cells and the remainder lymphocytes. The bone marrow showed hematopoiesis, with a definite reduction in the reticulocyte series. The megakaryocytes appeared normal. The ratio of immature red cells to immature white cells was 2 to 1. Because of the leucopenia, three transfusions were given, each of 250 cc. of Type O Rh-negative blood similar in type to that of the infant. This immediately raised the values to 12 gm. of hemoglobin, 3,800,000 red blood cells, and 3,100 white blood cells in 24 hours. During the remainder of life blood values were kept at 14.8 gm. of hemoglobin, 4,800,000 red blood cells, and 3,700 white blood cells by three similar transfusions. None of these transfusions increased the total number of white cells or changed the percentage of the differential white blood cell content.

The prothrombin time was 50% of normal. Cholesterol measured 124 mg. Electrophoretic studies for protein fraction showed possible cryoglobulinemia; with ether extraction, the sample contained 61% albumin, 9.0% alpha globulin, 9.9% alpha$_2$ globulin, 11.1% beta globulin, and 9.0% gamma globulin. The albumin globulin ratio was 1.53.

Throat cultures showed 4+ Streptococcus viridans. The blood cultures were negative. The urine had a 1+ reaction for albumin, and the roentgenograms of the long bones were normal. The electrocardiogram was within normal limits.

Pathological Report on Biopsy Specimen (Dr. George H. Haas, Chief of Department of Pathology).—The biopsy specimen included all layers of the skin and penetrated deeply through a layer of superficial facia into the subcutaneous adipose tissue. There were no significant changes in the epithelium of the skin. The corium was edematous. A few macrophages were present around lymphatics and dilated small blood vessels, especially those adjacent to sebaceous and sweat glands. The first evidence of conspicuous inflammation was at the junction of the connective tissues of the corium with the subjacent adipose tissues (Fig. 1). Here there was an intense inflammatory reaction which extended along the connective tissue septa and between individual fat cells into the deeper tissues. The inflammatory reaction diminished in intensity as the deep base of the biopsy specimen was approached (Fig. 2).

The general impression was that the reaction was in the nature of a subacute cellulitis of adipose tissue and its collagenous investment. Capillaries were dilated and occasionally were occluded by fibrinous thrombi. Macrophages and lymphocytes were numerous. Polymorphonuclear cells and eosinophiles were surprisingly infrequent. Exudation of plasma and fibrin was noticeable in many areas. Indeed, the eosinophilic homogeneous ring about the periphery of many fat cells seemed to consist partly of degenerative cytoplasm of macrophages which had

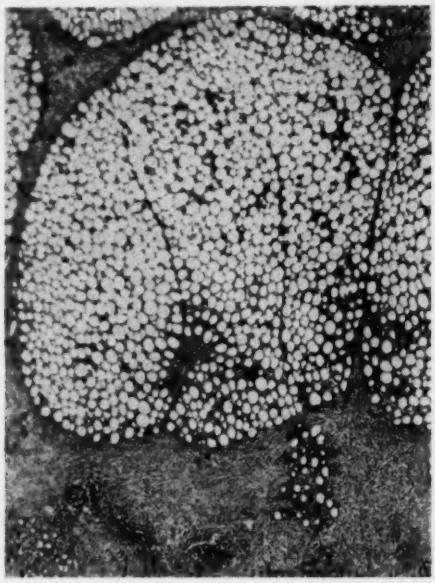

Fig. 1.—Low-power view of connective tissue of corium and subjacent subcutaneous fat tissue. There is a wide-extending inflammatory reaction in connective tissue of corium, along septa between lobules of fat, and in fat tissue proper.

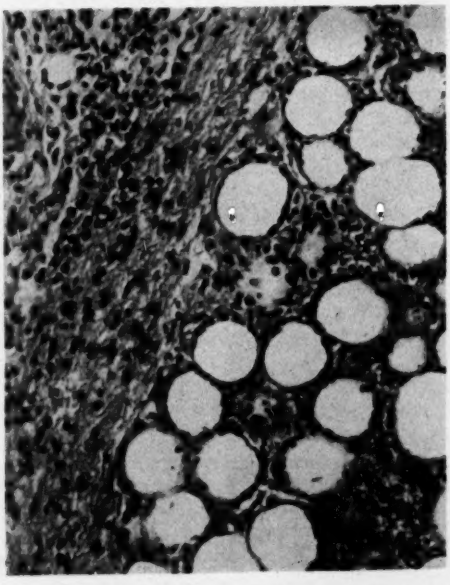

Fig. 2.—Medium-power illustration of adipose tissue adjacent to one of tubules shown in Figure 1. This view demonstrates infiltrating inflammatory cells in connective tissue. These are extending between fat cells. Fat cells show early necrosis, with fibrinoid type of degeneration in tissue between them.

encapsulated the degenerating fat cells. Crystal clefts and foreign-body reactions with the type of multinucleated giant cells so commonly seen in most forms of fat necrosis were absent. Sections stained by the methods of Giemsa, Gram, and Ziehl-Neelsen disclosed no bacteria.

It may be concluded that the changes were compatible with a diagnosis of subacute panniculitis of the Weber-Christian type. However, a specific microscopic diagnosis of Weber-Christian disease could not be made.

Bacteriologic Report.—Anaerobic and aerobic blood cultures were done on two different occasions, using brain broth, Brewer's thioglycollate broth, and blood-agar. There was no growth. The bacteriologic specimen consisted of a piece of subcutaneous tissue. This was ground in sterile sand and isotonic sodium chloride solution and cultured on blood-agar, chocolate-proteose agar, Brewer's brain broth, and Sabouraud's medium both aerobically and anaerobically. All cultures were negative in 24 hours. After 48 hours small colonies appeared on the chocolate-proteose agar from the anaerobic jar. All other cultures still remained negative.

These colonies, when stained by Gram's method, were observed to be Gram-positive cocci in chains. This organism was transferred from chocolate-agar to blood-agar and brain-heart dextrose broth. After this passage, Str. viridans grew both anaerobically and aerobically. Sensitivity tests were done and showed the following reactions: streptomycin, slight; penicillin, 2+; sulfadiazine, 4+; chloramphenicol, 4+; and aureomycin, 4+.

Hospital Course.—After the initial throat culture and blood work, injections of corticotropin (ACTH), 15 mg. every six hours, were begun. The temperature fell almost to normal; however, on the third day, it rose to 103 F. Three hundred thousand units of repository penicillin was then given daily. The fever subsided for two days. Sulfadiazine, 7½ grains (0.5 gm.) every eight hours, was then given. The following day the temperature rose to 102 F. On receipt of the bacterial report on the tissue culture, chloramphenicol, 250 mg., was given every six hours until death three days later. The temperature remained at 103 F.

In the interval between admission and death after 10 days, the baby continued to eat and drink fairly well; however, he became more irritable and lethargic. The skin lesions did not show any perceptible improvement with the various medicaments. In fact, new lesions were seen to develop on both elbows and in the mid-abdomen as irregular, nontender, nonelevated discolorations which were light pink.

The baby became more lethargic the last 24 hours of life. The skin became mottled; respirations were elevated to 60 to 80 per minute and the heart rate to 200 per minute. He suddenly died on the 10th day of hospitalization. Permission for autopsy was not given by the parents.

COMMENT

The medical literature on this condition was reviewed in 1949 by Bendel,[5] who has made an excellent table of the authentic cases. Shuman[6] again reviewed the literature in 1951 and added some instances from the foreign literature and several others that were not definitely included before. This is the reason for the discrepancy between his number of recorded instances, 54, and Bendel's, 43. Since this time another case has been reported by Eisaman and Schneider.[7] This with Shuman's case and our own case brings the total of recorded cases to date to 57.

The majority of these have been in adults, only eight children under 11 years of age being in this group. Of these children, four were girls between the ages of 8 and 11 years and four were boys, aged 2 years, 23 months, 8½ months (our

5. Bendel, W. L., Jr.: Relapsing Febrile Nodular Panniculitis (Weber-Christian Disease), Arch. Dermat. & Syph. **60**:570 (Oct.) 1949.

6. Shuman, C. R.: Relapsing Panniculitis (Weber-Christian Disease), A. M. A. Arch. Int. Med. **87**:669 (May) 1951.

7. Eisaman, J. L., and Schneider, L. A.: Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), J. A. M. A. **146**:1417 (Aug. 11) 1951.

patient), and 6 months.[8] Our patient is the youngest reported on in the American and English literature.

Many variations from the original clinical description have been reported, and attempts have been made to clarify this entity by Keil [9] in England and by Bailey [10] in this country. Bailey stated that little agreement had been reached on the conditions that should be considered under the title of panniculitis. He concluded that the term should encompass all pathological states in which subcutaneous fat is involved. He thought that Weber-Christian disease was a subgroup and considered it as an entity. In his opinion, therefore, it had to be differentiated from other diseases which involved fat.

However, all recorded cases have one major feature in common, involvement of subcutaneous fat alone. The observations suggest that a subtle change occurs in the fat, accompanied with an inflammation, the chief feature of which is the removal of the fat by phagocytosis without visible hydrolysis. Whether the inflammation initiates the process or is the result of changes in the fat alone is not clear. However, as will be seen from a review of the etiological factors, the condition might better be considered a syndrome than a disease.

As an example of this we have the blood picture. There is no great change in the blood except an occasional leucopenia, and it is not frequent. It has been reported in 10 instances including our own.[11] It certainly should not be included as a characteristic finding in this condition.

Many attempts have been made to demonstrate some definite etiological factor for the panniculitis. Focal infections have been observed in dental cavities and in tonsils.[12] However, in none of these instances were any blood cultures noted to yield pathogens, nor were the subcutaneous nodules found to contain bacteria. In two instances [13] death was thought to be due to a bacteremia with Streptococcus

8. (*a*) Gilchrist and Ketron.[8] (*b*) Cummins, L. J., and Lever, W. F.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian's Disease), Arch. Dermat. & Syph. **38**:415 (Sept.) 1938. (*c*) Hazel, O. G., and Lamb, J.: Primary Panniculitis, J. Oklahoma M. A. **33**:1 (Jan.) 1940. (*d*) Larkin, V. de P.; De Sanctis, A. G., and Margulis, A. E.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Am. J. Dis. Child. **67**:120 (Feb.) 1944. (*e*) Pinetti, P.: La malattia di Christian-Weber: Pannicolete nodular non suppurativa recidivante e febrile, Gior. ital dermat. e sif. **82**:297, 1941. (*f*) Carol, W. L. L.; Prakken, J. R., and van Zwijndregt, H. A.: Erythema Nodosum and Relapsing Febrile Nodular Nonsuppurative Panniculitis, Arch. Dermat. u. Syph. **182**:329, 1941.

9. Keil, H.: Panniculitis, Its Place in Nosology, Brit. J. Dermat. **47**:512 (Dec.) 1935.

10. Bailey, R. J.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), J. A. M. A. **109**:1419 (Oct. 30) 1937.

11. (*a*) Christian.[4] (*b*) Bailey.[10] (*c*) Brill, I. C.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), in Medical Papers Dedicated to Henry Ashbury Christian, Baltimore, Waverly Press, Inc., 1936, p. 694. (*d*) Friedman, N. B.: Fatal Panniculitis and Autopsy, Arch. Path. **39**:42 (Jan.) 1945. (*e*) Ives, G.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, J. Missouri M. A. **42**:409 (July) 1945. (*f*) Zee, M. L.: Nodular Nonsuppurative Panniculitis Treated with Penicillin, J. A. M. A. **130**:1219 (April 27) 1946. (*g*) Bunnell, I. L., and Levy, D. S.: Weber-Christian's Disease, Ann. Int. Med. **28**:169 (Jan.) 1948. (*h*) Johnson, W. A., and Plice, S. G.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Arch. Path. **48**:281 (Oct.) 1949. (*i*) Rosenberg, W. A., and Cohen, T. M.: Relapsing Febrile Nonsuppurative Panniculitis, Illinois M. J. **81**:59 (Jan.) 1942.

12. Pfeifer.[2] Cummins and Lever.[8b]

13. Ungar, H.: Relapsing Febrile Nodular Inflammation of Adipose Tissue, J. Path. & Bact. **58**:175 (April) 1946. Friedman.[11d]

hemolyticus and Staphylococcus pyogenes var. aureus, respectively. A disseminated tuberculosis was seen at autopsy in another instance.[14]

Puente,[15] in Uruguay, was the only other author to report an organism recovered from one of the nodules. This was a Staphylococcus. In our patient the organism recovered from a nodule was Str. viridans, which was also found in cultures from the throat. This organism could easily have been missed, if anaerobic cultures had not been made from the nodule. It is also interesting to note that this organism was almost insensitive to penicillin, which was the antibiotic used in the initial treatment.

Other etiological factors have been considered. In 10 reported instances there was a history of the administration of iodides and bromides before the lesions developed. These cases are all reported in the older literature. In one instance [11i] lesions cleared when iodide therapy was withdrawn, with reappearance when therapy was recontinued. In another instance [16] the patient had received injections of hormones, and also injections for allergy, before the disease developed. In five instances [17] the nodules developed after trauma at the site of the lesion. The injections of animal or vegetable oils and insulin [18] have all been considered as contributing factors. Bendel [5] is of the opinion that the condition is an allergic manifestation. We feel that Netherton's [19] suggestion that the local lesion may be caused by blood-borne chemicals or blood-borne bacteria, and that the nodule in reality is a metastatic lesion, may have some validity.

In diagnosing the condition, besides the clinical symptoms mentioned, and the microscopic appearance of the nodules, attempts have been made to find one characteristic laboratory finding. Several of the later authors have stated that the sedimentation rate is elevated. However, this might be expected with a persistent fever. Shuman [6] found that a reduction of adrenal cortex function was suggested by the finding of low 17-ketosteroid excretion, positive reactions to Robinson-Power-Kepler water tests, and failure of hyaluronidase inhibition after epinephrine administration. We should like to mention our own finding of cryoglobulinemia. It has been observed in only this one instance, but we believe it deserves some consideration.

The presence of a cryoglobulin, that is to say, a globulin precipitable by cold alone, was initially suggested by the creamy opacity of the child's serum, which on centrifugation still gave an opaque layer that in the electrophoretic cell at the usual

14. Tilden, I. L.; Gotshalk, H. C., and Avakian, E. V.: Relapsing Febrile Nonsuppurative Panniculitis, Arch. Dermat. & Syph. **41**:681 (April) 1940.

15. Puente, J. J.: Panniculitis nodular recidivante febrile de origen estafilocòccico, Rev. uruguaya dermat. y sif. **3**:52, 1938.

16. Madden, J. F.: Nonsuppurative Panniculitis, Arch. Dermat. & Syph. **59**:365 (March) 1949.

17. Brill.[11c] Shuman.[6] Baumgartner, W., and Riva, G.: Pannikulitis, die herdförmige Fettgewebsentzündung, Helvet. med. acta (Supp. 14) **12**:3, 1945. Fraser, J. F.: Nonsuppurating Panniculitis (Weber-Christian), Arch. Dermat. & Syph. **45**:810 (April) 1942. Miller, J. L., and Kritzler, R. A.: Nodular, Nonsuppurative Panniculitis, ibid. **47**:82 (Jan.) 1943.

18. Avery, H.: Insulin Fat Atrophy: A Traumatic Panniculitis, Brit. M. J. **1**:597 (March 30) 1929.

19. Netherton, E. W.: Relapsing Nodular Nonsuppurative Panniculitis, Brit. J. Dermat. **47**:512 (Dec.) 1935.

temperature of 0 C. precipitated, but at 10 C. gave the following results: albumin, 61%; alpha$_1$ globulin 9%; alpha$_2$ globulin, 10%; beta globulin, 11%, and gamma globulin, 9%.[20]

It is known that cryoglobulins are not present in normal serum in any significant amount.[21] They have been described in a considerable variety of adult diseases, such as lymphatic leukemia, bronchiectasis, and rheumatic fever.[22] The level giving rise to clinical symptoms and purpura and to the pathological findings of precipitated protein in superficial vessels is again uncertain. Levels both as low as 18 mg. per 100 cc. and as high as 8 gm. per 100 cc. have been associated with such findings.

The lipemic appearance of the plasma of this patient toward the end of his disease has been described in instances of cryoglobulinemia of excessive degree, and when no obvious explanation for this appearance of serum exists the presence of cryoglobulins should be suspected. Certain examination of serum for cold-precipitable proteins in a variety of obscure inflammatory conditions is indicated to yield an answer to the question of their primary or secondary role in the pathogenesis of the phenomena seen in association with cryoglobulinemia.

In the differential diagnosis one must first consider those conditions that cause changes in the subcutaneous fat tissues. Similar pathological pictures with dissimilar clinical features can be produced by various agents. Sclerema neonatorum and subcutaneous fat necrosis of the newborn can be excluded by the age of the child, as recovery, if it takes place, does so by the fourth or fifth month. Pathologically one finds necrosis of the subcutaneous fat beneath the involved areas. Localized atrophy of subcutaneous fat has occurred in persons with diabetes after the injection of insulin.[23]

On the other hand, certain diseases may simulate Weber-Christian syndrome clinically but may be entirely different pathologically. The subcutaneous fat nodules of adiposis dolorosa may resemble the nodules of Weber-Christian syndrome. Erythema nodosum, erythema induratum, and subcutaneous sarcoid of the Darier-Roussy type may resemble the initial lesion, but the nodules in these diseases do not progress to atrophy of the fat without changes in the skin. The lesions of morphea and circumscribed scleroderma are plaque-like, are slow to develop, and regress leaving the skin shriveled and bound to the underlying tissues.

The skin lesions would be compatible with dermatomyositis, as would the leucopenia, fever, and malaise. However, there was no muscle tenderness, dysphagia, or respiratory difficulty. The principal pathological changes are in the corium and voluntary muscles, while the subcutaneous fat is seldom, if ever primarily involved.

Lastly, disseminated lupus erythematosus should be considered from the standpoint of the systemic symptoms, including leucopenia and albuminuria, in the

20. Dr. S. Howard Armstrong, Chairman of the Department of Medicine, provided this discussion on cryoglobulinemia.

21. Morrison, P. R.; Edsall, J. T., and Miller, S. G.: The Separation of Purified Fibrinogen from Fraction I of Human Plasma, J. Am. Chem. Soc. **70**:3103 (Sept.) 1948.

22. Barr, D. P.; Reader, G. G., and Wheeler, C. H.: Cryoglobulinemia: I. Report of 2 Cases with Discussion of Clinical Manifestations, Incidence and Significance, Ann. Int. Med. **32**:6 (Jan.) 1950.

23. Rowe, A. H., and Garrison, O. H.: Lipodystrophy: Atrophy and Tumefaction of Subcutaneous Tissue Due to Insulin Injections, J. A. M. A. **99**:16 (July 2) 1932.

presence of disseminated skin lesions. However, in this condition the skin lesions are not indurated and the subcutaneous fat is not involved. The histopathological changes are in the epidermis and corium and occasionally in striated muscle. Furthermore, the age of this child would make the condition an extreme rarity.

There is no definite treatment for Weber-Christian syndrome. Corticotropin, cortisone, antihistaminic drugs, and the antibiotics have been used without lasting effect. Remission has been induced by x-ray therapy [6] and sulfapyridine administration.[24] Two authors have also obtained remissions with penicillin treatment.[25] Supportive therapy with a high-protein diet and a high-caloric diet with vitamins may be beneficial. Therapy with iron, protein, and testosterone has failed to influence the anemia. Salicylates have been given to alleviate the pain.

The disease is not particularly fatal. Only about a dozen of the patients have died of various causes, and only two deaths have been attributed to the panniculitis itself. Of these patients, seven have been studied at autopsy, with the following causes of death: tuberculosis, glomerulonephritis, pyogenic infection, peritonitis, Hodgkin's disease, and fatty infiltration of the liver. One patient [11d] died of a Staphylococcus septicemia. Whether our patient died from Str. viridans septicemia or from toxicity produced by the widely spread panniculitis is not known. Although blood cultures yielded no organisms, it is possible that septicemia was the cause of death. Unfortunately, since there was no autopsy, this will not be known.

CONCLUSIONS

A fatal case of chronic nonsuppurative panniculitis with leucopenia (Weber-Christian syndrome) is reported in an 8½-month-old infant. This is the youngest child reported on in the American and English literature. There have been eight recorded instances in children under 11 years of age in the medical literature. There has been a total of 57 cases reported in persons of all ages in the medical literature.

This is the second recorded instance in which a bacterial organism (Streptococcus viridans) has been cultured from the subcutaneous nodules and may have been the etiological agent.

We wish to call attention to the cryoglobulinemia, which may be of diagnostic importance.

From a review of the published descriptions of these cases, we believe that the disorder of Weber and Christian should be considered as a syndrome and not as a definite disease. It apparently occurs in conditions in which the subcutaneous fat is involved without suppuration. The etiological agent may be any one of many factors.

952 N. Michigan Blvd. (Dr. Sanford and Dr. Eubank).

1811 W. 47th St. (Dr. Stenn).

24. Arnold, H. L.: Nodular Nonsuppurative Panniculitis, Arch. Dermat. & Syph. **51**:94 (Feb.) 1945.

25. Zee.[11f] Livingstone, R. G.: Chronic Recurrent Suppurative Panniculitis Migrans, New York J. Med. **47**:1609 (July 15) 1947.

ORGANIC-ACIDURIA, DECREASED RENAL AMMONIA PRODUCTION, HYDROPHTHALMOS, AND MENTAL RETARDATION

A Clinical Entity

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THE OCCURRENCE of children with anomalous metabolic disturbances is distressing to parents and perplexing to physicians. However, such children frequently offer an opportunity for investigation that cannot be provided by animal experimentation. The following patients had abnormalities of renal function, bone disease, mental retardation, and congenital glaucoma. This combination appears to be unique, for we have been unable to find reports of similar children. Their cases are summarized briefly below and are presented in detail in an appendix.

SUMMARY OF CASES

PATIENT 1 (MGH 563342).—R. P., a 2-month-old infant, was examined because of bilateral congenital cataracts and was also found to have bilateral glaucoma, albuminuria, and minimal glycosuria. From 6 to 12 months of age he received calcium lactate and sodium lacate therapy. Intensively studied when one year old (Fig. 1), he was free of bone disease but had chronic serum acidosis, organic-aciduria, decreased ability to make urinary ammonia, mental retardation, and a piercing cry. Withdrawal of alkaline therapy permitted the development of rickets and appropriate changes in the calcium, phosphorus, and phosphatase concentrations of the blood.

PATIENT 2 (MGH 457905).—D. M., a 7-month-old infant, was found to have bilateral glaucoma, leucomas, and cataracts. When studied at 4 years of age, he was mentally retarded and areflexic. Urine contained albumin (1 to 2+), and roentgenograms of the bones showed demineralization but no rickets. Hyperchloremia and decreased serum carbon dioxide content were demonstrated. Also exhibited were pathological organic-aciduria and decreased urinary ammonia production.

PATIENT 3 (MGH 432873).—J. R., a 6-month-old infant, was found to have bilateral glaucoma and nuclear cortical cataracts. Also noted were a 4+ reaction for albumin and a 1+ reaction for sugar in the urine. At 3 years of age he was severely retarded mentally and had areflexia and a high-pitched, piercing cry (Fig. 2). Upon numerous occasions he was found to have serum acidosis and hypophosphatemia, an organic-aciduria, and low urinary ammonia production. Multiple fractures of his long bones and active rickets developed (Fig. 3, upper). The bone disease, though unaffected by vitamin D therapy alone, was improved by adding calcium and sodium salts to the therapeutic regimen (Figs. 3 and 4, lower parts).

From the Department of Pediatrics, Harvard Medical School, and the Pediatric Service of the Massachusetts General Hospital.

SUMMARY OF RESULTS OF PHYSICAL EXAMINATIONS

These patients shared the following physical abnormalities: hyperactivity, severe mental retardation, hyporeflexia, and flabby musculature with an abundance of subcutaneous fat (thus producing children who were relatively fat for their length). Two children had prominent frontal bossing. Each child had hydroph-

Fig. 1.—Patient R. P. at one year of age.

Fig. 2.—Patient J. R. at 3 years of age.

thalmos, and cataracts were present in two of the children. The hydrophthalmos was undoubtedly due to anomalies in the canal of Schlemm in the two children with cataracts, and in the third it was due to synechiae between the iris and the lens; accompanying the hydrophthalmos were steamy corneae and, as concomitants of this, blindness and a gross searching nystagmus. A peculiar, high-pitched,

irritating cry was present in all three children. The blood pressure was normal in each patient. Finally, the course of each child was characterized by intermittent fever without obvious cause.

SUMMARY OF ELECTROLYTE VALUES OF THE BLOOD

From examination of Table 1 it may be observed that the following chemical values characterize the peripheral blood of each patient: The carbon dioxide content was uniformly low. In one child the alkaline phosphatase was normal; in

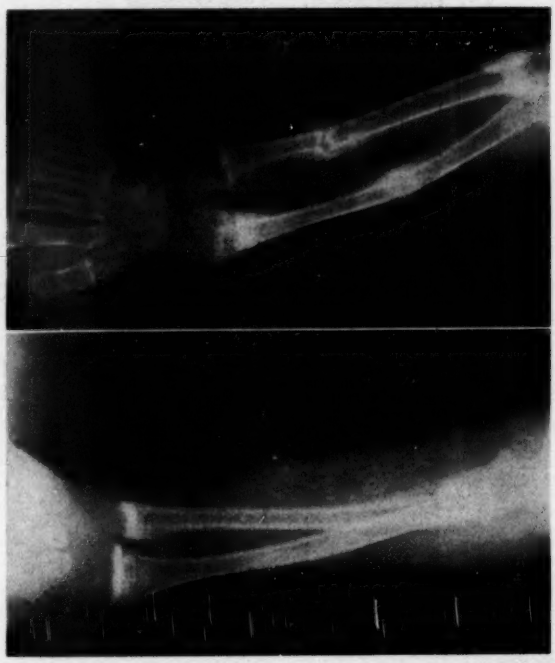

Fig. 3.—Roentgenograms of wrists of Patient J. R. (upper, made Feb. 12, 1947; lower, made March 18, 1947). Upper view shows poor healing of rickets and fractures which occurred while patient received 50,000 I.U. of vitamin D a day. When calcium lactate and sodium citrate were added to therapy, healing ensued, as shown in lower view.

TABLE 1.—*Laboratory Data on Blood Serum**

Patient	R. P.	D. M.	J. R.	Normal
pH	7.3	.....	7.2-7.3	7.4
Sugar, mg./100 ml.	85	.....	70	70
Chloride, mEq./L.	104-111	108	101-115	104
Phosphate, mg./100 ml.	4.1-6	4.4-6.5	1.1-5.5	5-6.6
Calcium, mg./100 ml.	8-11	9.1-10.2	8-11.4	10-10.5
Sodium, mEq./L.	133-140	140-143	135-142	136-145
Potassium, mEq./L.	4.4	4.7	2.1-5.7	3.5-5.0
Alpha amino nitrogen, mg./100 ml.	4.5	.....	3.5	3.4-5.5
Nonprotein nitrogen, mg./100 ml.	18-40	25-50	21-64	15-40
Phosphatase, Bodansky units/100 ml.	6.5-23	7.8-9.9	14.5-43	6-10
Carbon dioxide, mEq./L.	18-21.3	21-23.9	14.7-21.3	20-28
Magnesium, mEq./L.	1	.....	2.2	1-2

* Range observed throughout hospital course, excluding any values determined while patients were receiving ammonium chloride.

the second it was increased during periods of active bone disease; in the third it was always elevated. The chloride was either elevated or at the upper limits of normal. The inorganic phosphate was low to normal. The nonprotein nitrogen was normal except during sporadic periods of dehydration. Serum protein was

Fig. 4.—Roentgenograms of wrists of Patient J. R. (upper, made April 22, 1948; lower, made June 12, 1948), demonstrating recurrence of rickets while patient received no vitamin D and cure of bone disease when vitamin D (50,000 I.U. a day), calcium lactate (50 mEq. of calcium a day), and sodium citrate (62 mEq. of sodium a day) were added to the therapeutic regimen.

low or normal. Calcium was uniformly at a normal level. Sodium was low or normal. The pH of the blood was always below normal. Finally, the fasting levels of sugar and the alpha amino acids were normal.

SUMMARY OF ROENTGEN FINDINGS

In each instance roentgenograms of the bones of these children showed decreased opacity to x-rays. In Patient J. R. outright rickets was present. Moder-

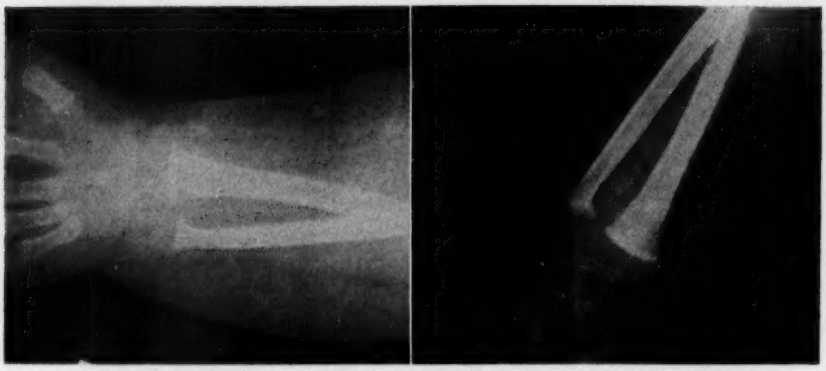

Fig. 5.—Roentgenograms of wrists of Patient R. P. (left, made Nov. 29, 1947; right, made May 8, 1948), demonstrating alteration that occurred when administration of calcium lactate (35 mEq. of calcium a day) was discontinued but vitamin D therapy (1,500 I.U. a day) was continued. Left view shows essentially normal bones, while right demonstrates advent of rickets. Increase in alkaline phosphatase of blood also occurred at this time.

Fig. 6.—Wrist of Patient D. M. on March 2, 1948. No active rickets is present, but some demineralization is apparent.

ate doses of vitamin D and added base therapy caused the lesions to heal. Each time medication with basic salts was discontinued rickets recurred (see Figs. 3 and 4). R. P., the first child, had received large doses of calcium lactate and

sodium lactate from 6 to 14 months of age. It seems probable that because of the fortuitous administration of base no bone disease had occurred in that eight-month period (Fig. 5, left). Furthermore, while receiving adequate amounts of vitamin D but no salt supplement, he twice exhibited active rickets (Fig. 5, right). The second patient, D. M., at no time exhibited active rickets (Fig. 6). Two explanations seem possible: (1) his almost complete lack of longitudinal growth during the period of study and (2) the fact that his renal abnormalities were the least severe of the three, i. e., his output of organic acid was much less than that of the other two children.

TABLE 2.—*Laboratory Data on Urine*

Patient	R. P.		D. M.		J. R.		
Weight	8,500 gm.		13,200 gm.		15,000 gm.		
Date	5/14	5/12	3/3	3/15	4/21	4/26	
Type of Collection	Control	50 mEq. NH_4Cl	Control	50 mEq. NH_4Cl	Control	50 mEq. NH_4Cl	Normal
Values/24 hr.							
Volume, ml.	325	450	355	435	392	260	.....
pH	7.75	6.04	5.7	5.5	5.4	6.45	.....
Acetone reaction	0	0	+	0	+	0	.....
Sugar reaction	0	0	±	0	0	+	.....
Ammonia, mEq.	4.84	14.3	14.1	14.8	16.98	14.4	.....
	3.2%*	5.5%*	6%*	12%*	6%*	6.6%*	4%*
	1.42†	.....	1.17†	1.75†	0.92†	3.58†	1-2.5†
Chloride, mEq.	12.35	38.25	16.46	69	18.3	43.2	.....
Phosphate, mEq.	15.7	21.5	22.1	3.71	28.5	14.0	{40%‡ {50%
Calcium, mEq.	0.268	1.98	1.035	2.94	1.76	1.85	1§
Sodium, mEq.	29.1	0.77	14.4	35.1	23.8	4.6	.....
Potassium, mEq.	22.3	33.2	33	38.1	30.5	41.5	.....
Titratable acid, mEq.	3.4	.....	12.0	8.84	18.2	4.68	.....
	(12/2)						
	0.4/kg.	.....	0.9/kg.	0.63/kg.	1.2/kg.	0.27/kg.	0.2-0.8/kg.
Alpha amino nitrogen, mg.	80	121	77	45	147	250	.....
	3.8%‖	3.2%‖	7.7%‖	3.85%‖	3.7%‖	7.5%‖	2%‖
	10%¶	27%¶	9%¶	18%¶	13.5%¶	42%¶	2%¶
Total nitrogen, gm.	2.15	3.89	3.15	1.85	3.97	3.19	.....
Nonprotein nitrogen, gm.	2.09	3.78	1.24	1.73	3.53	2.87	.....
Protein nitrogen, gm.	0.06	1.2	1.91	0.12	0.44	0.32	.....
Organic acid, mEq.	53.8	82.4	58.4	17.6	76.7	42.4	.....
	6.4/kg.	3.8/kg.	4.42/kg.	1.33/kg.	5/kg.	3/kg.	1/kg.
Creatinine, mg.	104	112	.....	.....	156	110	.....

* Per cent of total urinary nitrogen contributed by ammonia nitrogen.
† Ratio of milliequivalents of ammonia to milliequivalents of titratable acidity.
‡ Formula-fed infants. Per cent of total phosphorus intake excreted in urine. (Intake from 1,000 ml. of whole cow's milk is equal to about 52 mEq. per 24 hours.)
§ Formula-fed infants.
‖ Per cent of total urinary nitrogen due to alpha amino nitrogen.
¶ Per cent of milliequivalents of organic acids due to amino acids. Obtained by assuming that average molecular weight of the amino acids excreted is equal to 123 and that amino nitrogen is equal to 10.4% of total molecule. This value is at best an approximation. The method for organic acid determination, that of Van Slyke and Palmer,[2] depends upon titrating urine from pH 8 to 2.7. This will only partially measure amino acids, for most of the acidic ones have a pK value below 2.7, and the basic ones, above 8.0.

SUMMARY OF URINE FINDINGS

Reference to Table 2, which summarizes urine findings, will aid in the following discussion.[1]

Data on two types of collection are listed in Table 2: specimens obtained during control periods and those obtained during administration of ammonium chloride.

1. The laboratory methods used in this study have been previously summarized (Rourke and others: New England J. Med. **234**:24-28, 1946), or have been described by Peters and Van Slyke ("Quantitative Clinical Chemistry," Baltimore, Williams & Wilkins Company, 1931). The alpha amino nitrogen determinations were performed by Dr. Halvor N. Christensen.

The duration of administration of ammonium chloride was five days, and urine was collected for the last day of this period.

From volume data it can be seen that these patients did not have an obligatory polyuria. In each child urine could be concentrated above 1.018, and that of J. R. could be diluted to 1.005.

The pH of the urine, although frequently alkaline, could and did become acid in each child; but even under the influence of ammonium chloride administration the acidity was not extreme. This observation suggested an inability to excrete hydrogen ions.

Each child upon occasion did have acetonuria, though the reaction was never marked.

Two children, R. P. and J. R., had glycosuria upon one or more occasions. This finding was studied most accurately in J. R. During an oral dextrose tolerance test, when the level of blood sugar was 162 mg. per 100 ml., there was no glycosuria. Patient R. P. also had a normal oral dextrose tolerance curve. Upon a single determination the sugar in the urine of J. R. was fermentable, suggesting that it was glucose.

In the normal person, not under conditions of stress, the ammonia nitrogen amounts to about 4% of the urinary nitrogen.[2] Under the influence of acidosis it may increase tenfold. These patients were given ammonium chloride in an amount to yield 50 mEq. of chloride per 24 hours. This was continued for five days, and a 24-hour urine collection was obtained on the fifth day. In no instance was the elaboration of ammonia under the stress of chloride acidosis increased to amounts that a normal person would produce.[3] Patient D. M., who had the least evidence of disease, produced the largest amount of ammonia, when compared with total urinary nitrogen, but the absolute amount of ammonia did not increase.

The values for urinary nonprotein nitrogen were obtained only as reference standards for comparison with ammonia and alpha amino nitrogen excretion. The protein nitrogen output though abnormal, between 0.06 and 1.9 gm. per 24 hours, could easily be accounted for by failure of tubular reabsorption of protein.[4]

The excretion of chloride following the administration of ammonium chloride was considerably increased in all patients. Patient D. M. excreted the total amount of chloride ingested. The other two patients did not excrete an amount of chloride which approached the sum of the amount excreted on the control days plus the amount given as ammonium chloride. This suggests that there was some difficulty in the excretion of chloride (*vide infra*, paragraph on sodium output).

In normal persons under the influence of acidosis, phosphate excretion in the urine increases.[5] In our patients the increase did not occur. Although there was some fluctuation in phosphate intake, it would seem that the sharp lowering of phosphate following acidosis demonstrated by Patients D. M. and J. R. could

2. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931.

3. Gamble, J. L.; Blackfan, K. D., and Hamilton, B.: A Study of the Diuretic Action of Acid-Producing Salts, J. Clin. Invest. **1**:359-388, 1925.

4. Addis, T.: Glomerular Nephritis: Diagnosis and Treatment, New York, The Macmillan Company, 1949.

5. Haldane, J. B. S.: Experiments on the Regulation of the Blood's Alkalinity, J. Physiol. **55**:265-275, 1921.

not be accounted for by an equally large change in intake. This observation suggested an inability to utilize the phosphate mechanism to conserve fixed base.

The excretion of calcium in the urine of these patients was not remarkable for normal patients [6] but was possibly increased for patients with osteomalacia. J. R. upon one occasion excreted 5.7 mEq. per 24 hours, considerably more calcium than would a normal child; however, he was receiving large doses of vitamin D. Under the stress of acidosis, each patient responded with increased calcium excretion.

The renal excretion of sodium is largely a function of intake; therefore, absolute values mean little. The sodium output increased in Patient D. M. with acidosis, which is the expected change. In the other two patients, the sodium output in the urine dropped with acidosis, nor did the latter children excrete the anticipated amount of chloride in the urine after ingestion of 50 mEq. of ammonium chloride as noted above. The difference in urinary sodium between the control and the acidotic period is an amount in milliequivalents approximately equal to that of the missing chloride ion. If the sodium was retained in the body with the chloride (i. e., if the ability of the kidney to excrete chloride had been exceeded), one might suppose that these patients would have gained weight because of an accumulation of extracellular fluid. Unfortunately, measurements of weight are not available to support this hypothesis.

Similar to renal sodium output is renal potassium output; the intake largely determines the amount excreted. When there is a demand for fixed base by the kidney, it might be expected that the potassium output would increase. This phenomenon has been observed in adults with renal acidosis.[7] In the two patients in whom the sodium output decreased with acidosis, potassium excretion increased. In the third patient, the reverse was true.

The normal person excretes between 0.2 and 0.8 mEq. of titratable acidity per kilogram of body weight per 24 hours and under the stress of acidosis between two and four times as much.[8] It is obvious from inspection of Table 2 that our patients had an impaired ability to excrete a normal amount of titratable acid after chloride acidosis. A further measure of this impaired ability is the ratio between urinary ammonia and titratable acidity. In normal persons the ratio falls within the limits of 1 to 2.5.[9] Had our patients been able to excrete increasing amounts of hydrogen ion to preserve fixed base while unable to fabricate ammonia, this ratio would decrease considerably. If they were able to excrete normal amounts

6. Albright, F.; Consolazio, W. V.; Coombs, F. S.; Sulkowitch, H. W., and Talbott, J. H.: Metabolic Studies and Therapy in a Case of Nephrocalcinosis with Rickets and Dwarfism, Bull. Johns Hopkins Hosp. **66**:7-33, 1940.

7. Albright, F.; Burnett, C. H.; Parson, W.; Reifenstein, E. C., Jr., and Roos, A.: Osteomalacia and Late Rickets: The Various Etiologies Met in the United States with Emphasis on That Resulting from a Specific Form of Renal Acidosis, the Therapeutic Indications for Each Etiological Sub-Group, and the Relationship Between Osteomalacia and Milkman's Syndrome, Medicine **25**:399-479, 1946.

8. Fitz, R., and Van Slyke, D. D.: Studies of Acidosis: IV. The Relationship Between the Alkaline Reserve and Acid Excretion, J. Biol. Chem. **30**:389-400, 1917. Schiess, W. A.; Ayer, J. L.; Lotspeich, W. D., and Pitts, R. F.: The Renal Regulation of Acid-Base Balance in Man: II. Factors Affecting the Excretion of Titratable Acid by Normal Human Subject, J. Clin. Invest. **27**:57-64, 1948.

9. Van Slyke, D. D.; Linder, G. C.; Hiller, A.; Leiter, L., and McIntosh, J. F.: The Excretion of Ammonia and Titratable Acid in Nephritis, J. Clin. Invest. **2**:255-288, 1926.

of ammonia under the influence of acidosis but unable to excrete hydrogen ions, the ratio would increase. Since the ratio of ammonia to titratable acidity increased but slightly during acidosis in the two children in the urine of whom it was measured, and since the ammonia production did not change, there seems good reason to believe that they had impaired ability to excrete hydrogen ions for base conservation.

Pitts and co-workers [10] investigated the ability of dogs and men to excrete acid urine. By measuring the milliequivalents of acid contribution by phosphate and bicarbonate under conditions of acidosis, they demonstrated that neither substance was able to supply the hydrogen ions excreted in the urine under their experimental conditions. They proposed an ion-exchange mechanism whereby within the tubules a basic ion, associated with an organic acid, is exchanged for a hydrogen ion which had been associated with carbonic acid in the plasma. If this mechanism pertains to children, one might further assume that our patients had an inability to use it; they were unable to exchange basic ions for hydrogen ions across the tubular wall.

With the use of the ninhydrin method, the urinary alpha amino nitrogen normally accounts for less than 2% of the urinary nonprotein nitrogen.[11] However, we have been able to find no values for children from the literature based on use of this method. Albanese [12] gives a figure of 3 to 4%, using a different method. With the ninhydrin method of determination, our patients excreted more than 2% of their urinary nitrogen as alpha amino nitrogen and in several instances more than 7%.

While these total values may be equivocal, partition chromatograms (performed by Dr. Fredric C. Barter), made with the Dent [13] technique, revealed that qualitatively the amino acids excreted were abnormal (Fig. 7). The normal person may excrete glycine, alanine, valine, and leucine in his urine, at least as revealed by chromatography. Our patients each excreted 9 amino acids in their urine, and one of them excreted 10. Eckhardt and Davidson,[14] in studying normal adults, found that other amino acids could be excreted. But they determined the amino acids by microbioassay while Dent used chromatography. Therefore, according to Dent's method and figures, our patients excreted qualitatively abnormal amino acids. Furthermore, it can be calculated from McCune's data [15] that in the normal person approximately 2% of total organic acid ouptut in milliequivalents is accounted for as amino acids. Our patients at all times excreted much more than that but never

10. Pitts, R. F.; Lotspeich, W. D.; Schiess, W. A., and Ayer, J. A.: The Renal Regulation of Acid-Base Balance in Man: I. The Nature of the Mechanism for Acidifying the Urine, J. Clin. Invest. **27**:48-56, 1948.

11. Van Slyke, D. D.; MacFadyen, D. A., and Hamilton, P. B.: The Gasometric Determination of Amino Acids in Urine by the Ninhydrin-Carbon-Dioxide Method, J. Biol. Chem. **150**:251-258, 1943.

12. Albanese, A. A., and Irby, V.: The Determination of Urinary Amino Nitrogen by the Copper Method, J. Biol. Chem. **153**:583-588, 1944.

13. Dent, C. E.: The Aminoaciduria in Fanconi Syndrome: A Study Making Extensive Use of Techniques Based on Paper Partition Chromatography, Biochem. J. **41**:240-253, 1947.

14. Eckhardt, R. D., and Davidson, C. S.: Urinary Excretion of Amino Acids Following the Rapid Injection of a Solution of Amino Acids in Man, J. Clin. Invest. **27**:727-736, 1948.

15. McCune, D. J.; Mason, H. H., and Clark, H. T.: Intractable Hypophosphatemic Rickets with Renal Glycosuria and Acidosis (the Fanconi Syndrome): Report of Case in Which Increased Urinary Organic Acids Were Detected and Identified, with Review of the Literature, Am. J. Dis. Child. **65**:81-146 (Jan.) 1943.

approached the figure of 85% obtained from McCune's patient with the Fanconi syndrome. It would thus seem that we can appeal to three types of reasoning to confirm the existence of abnormal aminoaciduria.

The normal person excretes approximately 1 mEq. of organic acids per kilogram of body weight per 24 hours.[16] Our patients excreted between 1.3 and 6.4

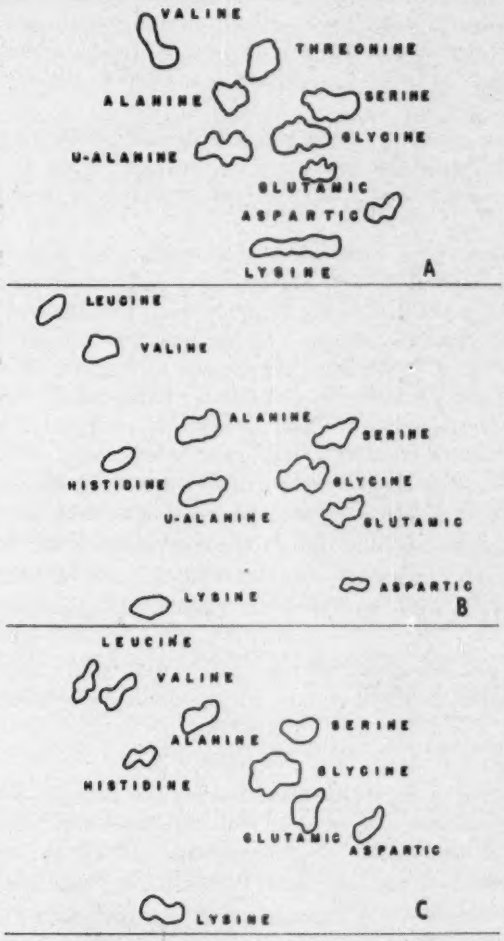

Fig. 7.—Amino acid chromatograms of urine: *A*, Patient R. P.; *B*, Patient J. R., and *C*, Patient D. M.

mEq. per kilogram of body weight per 24 hours. The patient with the Fanconi syndrome studied by McCune [16] had a considerable increase in organic acid excretion, and it was found that 85% of the organic acids, in milliequivalents, was accounted for by alpha amino acids. By obtaining the average molecular weight of amino acids

16. Van Slyke, D. D., and Palmer, W. W.: Studies of Acidosis: XVI. The Titration of Organic Acids in Urine, J. Biol. Chem. **41**:567-585, 1920.

excreted by our patients and knowing the total amount excreted per 24 hours, it was possible to arrive at a rough approximation of the contribution of these acids to the total amount of organic acids excreted per day. This type of calculation suggests that in no instance did the value for amino acid output approach the value for the total amount of the organic acids excreted. Since in each instance these children excreted between two and six times the normal amount of organic acids, some nonamino organic acid must have been present in abnormal amounts. That this acid was not beta-hydroxybutyric acid was proved by a negative reaction of the urine with ferric chloride. No attempt was made to look for such an acid in the blood.

Cystine is not ordinarily detectable with the use of Dent's chromatography. However, standard qualitative tests for cystine were performed, and negative results were found. It seems apparent that the organic-aciduria of these patients was not due to cystine.

Urea clearances, when obtained with adequate urine volumes, were always within the limits of normal. This finding, along with normal nonprotein nitrogen level in the blood and in the absence of an abnormal retention of phosphate, would tend to rule out glomerular disease. In one child (J. R.) phenolsulfonphthalein excretion was 40% in 40 minutes. Intravenous pyelograms were normal in each patient, suggesting good ability to concentrate; no evidence of renal calcification was seen by roentgenogram. Finally, numerous attempts to demonstrate the presence of chronic urinary tract infection were unsuccessful.

From the discussion above, it seems correct to assume that these patients had renal disease and osteomalacia. The first seems self-evident, and the second may need discussion. The following reasons would substantiate this diagnosis:

A. These patients chemically had osteomalacia—low to normal serum inorganic phosphorus, low to normal serum calcium, and elevated serum alkaline phosphatase.[16a]

B. By roentgenogram, two of them had active rickets which responded to therapy. It is unfortunate that no bone biopsy specimens were obtained to confirm this point.

COMMENT

With this outline of the clinical manifestations and chemical aberrations of these patients in mind, one can compare them with well-established types of renal disease and the causes of osteomalacia. It should then be possible to inquire whether the children's condition was the same as or different from these syndromes.

1. The investigation by Butler, Albright, and Bloomberg[17] of a child with rickets who had had adequate vitamin D intake by ordinary standards led to the elucidation of the syndrome of vitamin-D-resistant rickets. Patients with this disease respond only to notably high doses of vitamin D and have no obvious renal anomalies. The bony lesions in our patients responded to base therapy with modest doses of vitamin D; hence they did not have vitamin-D-resistant rickets.

16a. Albright, F. A., and Reifenstein, E. C., Jr.: The Parathyroid Glands and Metabolic Bone Disease, Baltimore, Williams & Wilkins Company, 1948.

17. Albright, F.; Butler, A. M., and Bloomberg, E.: Rickets Resistant to Vitamin D Therapy, Am. J. Dis. Child. **54**:529-547 (Sept.) 1937.

2. Owing at least in part to failure of absorption of vitamin D from their intestine, some children and adults with steatorrhea have active rickets or osteomalacia.[18] Tests done on Patient J. R. revealed normal fat absorption. This would seem to rule out steatorrhea as a cause of his osteomalacia and presumably that of the others by inference.

3. Boyd and Stearns [19] reported on four patients with late rickets. These children all had renal disease characterized in part by fixed urinary specific gravity, slight albuminuria, hyperphosphaturia, and intermittent glycosuria. The most striking feature other than the obvious bone disease, in three of the patients, was the low serum chloride concentration. The condition of each was improved with large doses of vitamin D and an oral intake of alkalinizing salts. Autopsy, in one instance, showed swelling of the tubular epithelium. Our patients had neither the low serum chloride nor the fixed urinary specific gravity characteristic of Boyd's patients.

4. Fanconi in 1936,[20] McCune and associates in 1943,[15] and others [13] have described a syndrome characterized by (*a*) active rickets, (*b*) glycosuria, (*c*) aminoaciduria, (*d*) hyperphosphaturia, (*e*) acidosis with ketonuria, (*f*) organic-aciduria, (*g*) albuminuria, and (*h*) increased urinary ammonia. In McCune's case, the amino acids accounted for 85% of the increased organic acids in the urine and ammonia produced was approximately 10 times the normal amount. The discrepancy between the ability to make ammonia of our patients and that of the patients of McCune and Fanconi would seem to divide the two groups of patients. Furthermore, in McCune's patient the organic-aciduria was largely due to amino acids, while this does not appear to be true in the present patients.

5. Butler, Wilson, and Farber [21] have reported clinical findings and observations on five children who had a bizarre systemic acidosis, polyuria, hyperchloremia, no albuminuria, and normal nonprotein nitrogen in the blood. Postmortem examination on three of the children revealed calcium phosphate gravel in the renal pelvis and pyramids. No active bone disease is reported. Since the present patients did not have an obligatory polyuria, gravel in their urine, or a serum chloride elevation of the magnitude described by Butler and associates, it seems doubtful that these entities are the same.

6. Cystinuria as a cause of rickets was emphasized by McCune.[15] In his classification he included under the Fanconi syndrome those cases in which there was obvious derangement in cystine metabolism. With the background of his collected

18. Albright and others.[7] Bassett, S. H.; Keutmann, E. H.; Hyde, H. V.; Van Alstine, H. E., and Russ, E.: Metabolism in Idiopathic Steatorrhea: I. The Influence of Dietary and Other Factors on Lipid and Mineral Balance, J. Clin. Invest. **18**:101-120, 1939. Parsons, L. G.: Celiac Disease: Rachford Memorial Lectures, Am. J. Dis. Child. **43**:1293-1346 (May, Pt. 2) 1932.

19. Boyd, J. D., and Stearns, G.: Late Rickets Resembling Fanconi Syndrome, Am. J. Dis. Child. **61**:1012-1022 (May) 1941; Concomitance of Chronic Acidosis with Late Rickets, ibid. **64**:594-607 (Oct.) 1942.

20. Fanconi, G.: Der frühinfantile nephrotisch-glykosurische Zwergwuchs mit hypophosphatämischer Rachitis, Jahrb. Kinderh. **147**:299-388, 1936.

21. Butler, A. M.; Wilson, J. L., and Farber, S.: Dehydration and Acidosis with Calcification at Renal Tubules, J. Pediat. **8**:489-499, 1936.

data, the interesting reports by Russell and his co-workers,[22] and the experience of Barter,[23] we may make the following divisions of this not uncomplicated problem:

A. There apparently are patients with cystinosis without cystinuria. They may suffer from any of the urinary abnormalities found in the Fanconi syndrome, particularly glycosuria and aminoaciduria. At autopsy cystine deposits are found throughout the reticuloendothelial system.[24]

B. There are other patients who have aminoaciduria, secreting cystine out of proportion to the other amino acids, but without cystinosis. They, too, are similar to patients with the Fanconi syndrome.

C. Finally, a group of patients has been described with a type of cystinuria which has its origin in an inborn error in metabolism.[25] These persons do not have rickets. Barter[23] and others have demonstrated that although it is the cystinuria in these patients that has come to the attention of physicians these patients have other amino acids in their urine. It is the relative insolubility of cystine and the occurrence of cystine stones and stag-horn calculi that led to the designation of the disease as cystinuria. Conceivably, with long-standing calculi these patients might display evidence of tubular insufficiency, but, in general, their condition should not be classed with the other causes of renal disease and osteomalacia. Of the three patients described by Russell and colleagues,[22] each apparently suffered from one of these three different forms of cystine disease. The existence in our patients of cystinuria seems doubtful in the absence of cystine on qualitative tests. No evidence for or against cystinosis has been advanced, but in a brief perusal of reported cases of cystinosis no descriptions have been found of patients with the associated anatomical anomalies present in our patients.

7. A syndrome characterized by tubular insufficiency without glomerular insufficiency has been shown to lead to bone disease.[7] The fundamental abnormality of these patients is an inability to fabricate ammonia in the renal tubules, and, as a consequence of this, there is a loss of fixed base from the body. As far as is known, this syndrome is idiopathic in origin. Although there are hyperphosphaturia and occasionally renal calculi, even leading to nephrocalcinosis, there is no increased output of organic acids as in several of the previously described syndromes. Since our patients had organic aciduria, this alone should differentiate them from Albright's patients.

8. One group of patients with tubular insufficiency but without glomerular disease may have, as the origin of their disability, chronic pyelonephritis. Albright[7] has described two patients of this sort, one of whom at autopsy had changes in the renal pelvis which were not out of keeping with those observed in chronic pyelonephritis. The late sequelae of this lesion are not unlike those described above in

22. Russell, D. S., and Barrie, H. J.: Storage of Cystine in the Reticulo-Endothelial System and Its Association with Chronic Nephritis and Renal Rickets, Lancet **2**:899-905, 1936.

23. Barter, cited by Albright and Reifenstein.[16a]

24. Looser, R.: Ein Fall von Cystinspeicherung mit renalem Zwergwuchs und Rachitis, Ann. pædiat. **163**:251-313, 1944.

25. Barter.[23] Looser.[24] Wolf, C. G. L., and Shaffer, P. A.: Protein Metabolism in Cystinuria, J. Biol. Chem. **4**:439-472, 1908.

syndrome 7 with eventual nephrocalcinosis. The evidence for chronic infection in our patients is poor, since most urine specimens were sterile. Furthermore, they had no evidence of nephrocalcinosis.

9. Primary hyperparathyroidism, at least initially, frequently leads to hyperphosphaturia and hypercalciuria, as well as bone lesions.[26] The bone lesions are those of osteitis fibrosa, not osteomalacia. These patients have none of the symptoms of those syndromes associated with tubular insufficiency without glomerular insufficiency, nor do they have those of the Fanconi syndrome. However, because of the increased urinary phosphate and calcium, interstitial calcification and deposition of calcium within the tubules, or even within the renal pelves,[27] may develop. Calculi may in turn lead to infection. It is conceivable that this might lead to tubular insufficiency without glomerular insufficiency. Thus, a patient, though relieved of a parathyroid adenoma, might display osteomalacia secondary to chronic pyelonephritis.

Did our patients have primary hyperparathyroidism? Certainly the plasma values for calcium and phosphorus were not similar to those usually observed in patients with hyperparathyroidism. Secondly, children with primary hyperparathyroidism usually do not have rickets.[16a] Thirdly, our patients had no renal calculi. Finally, no reference to organic-aciduria can be found in reports on patients with hyperparathyroidism. This reasoning would seem to suggest that our patients did not have either early or late primary hyperparathyroidism. Did they have secondary hyperparathyroidism? According to Albright,[29] in the presence of a kidney the base-conserving mechanisms of which are aberrant, the drain on serum calcium for use as urinary base leads to secondary hyperparathyroidism. It seems reasonable to suppose, then, that our patients had secondary hyperparathyroidism. This, however, probably played no role in the pathogenesis of their disease.

10. A final situation needs to be defined. Clinically, glomerular nephritis may terminally cause demineralization of the bones in children and adults. It is important to realize that this osseous disease, however, is not osteomalacia but rather osteitis fibrosis generalisata. The metaphyseal changes that develop may roentgenologically look like rickets, but microscopically they may be differentiated from that condition.[6] Metabolically these patients have a serum acidosis with retention of nitrogenous products and phosphate; the urine contains albumin, has a fixed specific gravity, and shows other evidence of decreased glomerular function. The normal nonprotein nitrogen and serum inorganic phosphorus, as well as the normal ability to dilute and concentrate urine, would seem to preclude this diagnosis in our patients.

On the basis of the above information it does not seem possible to include our patients' condition with any of these well-defined renal syndromes.

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26. Albright, F.; Baird, P. C.; Cope, O., and Bloomberg, E.: Studies on the Physiology of the Parathyroid Glands: IV. Renal Complications of Hyperparathyroidism, Am. J. M. Sc. **187**:49-65, 1934.

27. Albright, F.: Renal Osteitis Fibrosa Cystica: Report of a Case with Discussion of Metabolic Aspects, Tr. A. Am. Physicians **51**:199-212, 1936.

28. Footnote deleted.

29. Albright.[27] Albright and Reifenstein.[16a]

PATHOPHYSIOLOGIC ASPECTS

What reasons can be advanced to explain the various anomalies observed? Opacities in the eyes have been reported in hyperparathyroidism [30] and hypoparathyroidism,[31] as well as in cystinosis.[32] Descriptions of the cataracts in the present children (see appendix), however, would seem to indicate that they were not of the type seen in these conditions, since in the first instance the opacities are not lenticular, but rather subconjunctival; in the second instance they are the usual lenticular type; in the third they are due to cystine crystals which are corneal in location. Hydrophthalmos has not been reported as a complication of any of these three metabolic disturbances. Furthermore, a review of autopsies on patients with hydrophthalmos has failed to reveal any with renal disease.[33]

The organic acid excretion would suggest an inborn error in metabolism, possibly similar to that present in phenylpyruvic oligophrenia.[34] By inference this might suggest a cause for mental retardation. The excretion of increased urinary organic acids might be the first stage in the pathogenesis of bony lesions. Probably the degree of organic-aciduria present would not be enough to cause chronic acidosis; but when organic-aciduria is superimposed upon a kidney which is (*a*) unable to fabricate normal amounts of ammonia, (*b*) deficient in its ability to exchange basic for acid phosphate, and (*c*) unable to make the hydrogen-ion exchange postulated by Pitts,[10] it might explain the metabolic disturbances.

The recurrence of febrile episodes in these children, with no apparent cause, may excite speculation. We would like to believe that the fever was due to dehydration. Patients suffering from a chronic renal demand for fixed base may sacrifice as much extracellular base as they can and then excrete extracellular water to preserve osmotic equilibrium. Thus, they survive with decreased extracellular water, and any situation which increases the body's demand for water, even though the demand be for an amount well tolerated by a normal person, would cause fever as a manifestation of dehydration.

The glycosuria is most easily explained on the basis of poor tubular reabsorption.[35] It is possible that the aminoaciduria is supplementary evidence of tubular insufficiency of a selective sort. Certainly, since the blood levels of amino acids and glucose were normal, it would be impossible to postulate that the increased excretion arose from hyperglycemia or hyperaminoacidemia. Could the excretion of amino acids of a selected sort be related to the inability to make ammonia? It has been postulated that ammonia production in the kidney occurs through a

30. Walsh, F. B., and Howard, J. E.: Conjunctival and Corneal Lesions in Hypercalcemia, J. Clin. Endocrinol. **7**:644-652, 1947.

31. O'Brien, C. S.: Cataract of Postoperative Tetany, with Report of 3 Cases, Arch. Ophth. **7**:71-96 (Jan.) 1932.

32. Burki, E.: Über Augenveränderungen bei der Cystinkrankheit, Ann. pædiat. **156**:324-334, 1941.

33. Anderson, J. R.: Hydrophthalmia, or Congenital Glaucoma, London, Cambridge University Press, 1939.

34. Følling, A.: Über Ausscheidung von Phenylbrenztraubensäure in den Harn als Stoffwechselanomalie in Verbindung mit Imbezillität, Ztschr. Physiol. Chem. **227**:169-176, 1934.

35. Richards, A. N.: Processes of Urine Formation, Croonian Lecture, Proc. Roy. Soc., London, s. B **126**:398-432, 1938.

mechanism which catabolizes glutamine.[36] However, had the excess urinary alpha amino nitrogen been converted quantitatively to ammonia, it could not have supplied the deficiency of this ion during the periods of acidosis.

These features, along with the normal glomerular function as demonstrated by normal urea clearance and in spite of the ability to concentrate and dilute, might suggest that the renal lesion in these children was at least largely in the tubule.

Was there a specific inability to excrete chloride? Before answering the question, it might be well to speculate on the mechanism suggested by Darrow [37]

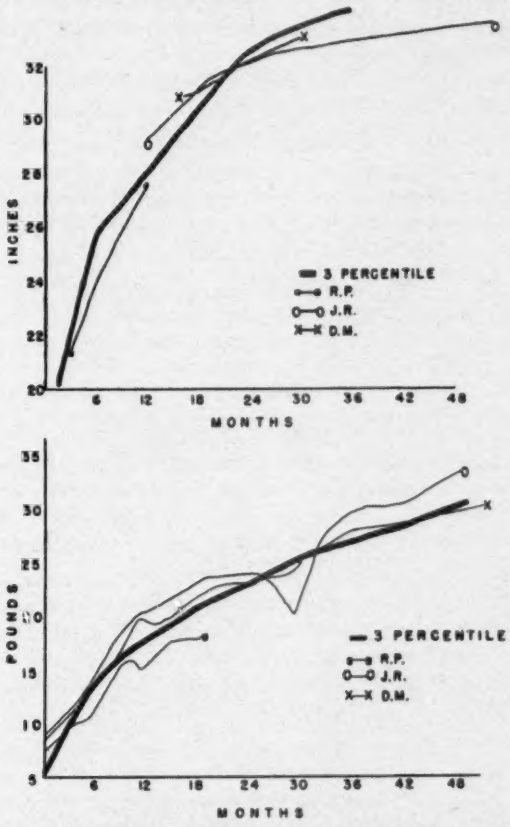

Fig. 8.—Charts showing longitudinal growth (upper) and weight (lower) of three patients. While patients grew poorly, they could not be classed as dwarfs; relatively, their weight was greater than their height, as compared with the third percentile of normal children.

that occurs in rats who are chronically alkalotic. In these animals, when the serum bicarbonate increases the intracellular sodium increases and the intracellular

36. Van Slyke, D. D.; Phillips, R. A.; Hamilton, P. B.; Archibald, R. M.; Futcher, P. H., and Hiller, A.: Glutamine as Source Material of Urinary Ammonia, J. Biol. Chem. **150**:481-482, 1943.

37. Darrow, D. C.; Schwartz, R.; Iannucci, J. F., and Coville, F.: The Relation of Serum Bicarbonate Concentration to Muscle Composition, J. Clin. Invest. **27**:198-208, 1948.

potassium decreases. Furthermore, there is a loss of serum chloride which cannot be ameliorated by the administration of chloride. But without the administration of chloride it readily rights itself on the administration of potassium. In other words, low muscle potassium would seem to cause low serum chloride. Chronic acidosis, on the other hand, produces a decrease in intracellular sodium and an increase in intracellular potassium, and with these an elevated serum chloride becomes necessary. In other words, these children, if Darrow's hypothesis may be extended, did not suffer from a renal inability to excrete chloride but rather had made a metabolic adjustment which is physiological for chronic acidosis. It is interesting to note that other patients with systemic acidosis have a high serum chloride concentration and a low level of serum potassium.[7]

The results of experiments undertaken to demonstrate the dependence of these patients on alkali given orally (see appendix) would seem to aid in reaching the conclusion that there was an abnormal drain on the body's supply of fixed base. The appearance of bone lesions during the periods without base therapy tends to confirm the fact that the excretion of organic acids was a drain upon the fixed base of the skeleton. There seemed to be no inability to lay down bone, since the addition of sufficient alkali therapy resulted in normal healing of the skeleton.

No microscopic studies are available on the patients reported herein. An attempt to find observations from autopsies at the Massachusetts General Hospital on other children who suffered from this disease was without success.

SUMMARY

Presented are the clinical histories of three patients with mental retardation, systemic acidosis, hydrophthalmos, organic-aciduria, and decreased ability to fabricate ammonia in the kidney. Without the aid of therapy two of them exhibited osteomalacia or rickets. An attempt has been made to compare these children with other persons suffering from rickets and renal disease. It has not been apparently possible to include their condition with any previously described syndrome. It is hypothesized that the condition may represent a previously unreported syndrome which has its pathogenesis in (1) an inborn error in metabolism producing excess organic acids for excretion and (2) impaired renal tubular function. Data have been presented to show that the children are dependent upon added base for the achievement of a normal skeleton and that vitamin D is at least partly able to assert its normal function.

APPENDIX

DETAILED CASE HISTORIES

PATIENT 1 (MGH 563342).—R. P. was born on Dec. 19, 1946. He was first seen at the Eye and Ear Infirmary of the Massachusetts General Hospital at 2 months of age, with the chief complaint of "congenital cataracts" of both eyes.

The mother and father were living and well. The patient was an only child. No familial history of metabolic diseases could be elicited, nor was there any evidence of consanguinity. The child was the product of a normal full-term pregnancy, terminating in spontaneous delivery. The mother's course was uneventful during pregnancy except for three days of vaginal bleeding during the fifth month. The birth weight was 3,500 gm. There was no history of neonatal distress, and in six days the infant had regained his birth weight. He was bottle-fed, ate without difficulty, and received 5 drops of a proprietary multivitamin preparation daily.

At 2 months of age he was an active, well-developed infant who weighed 4,100 gm. His head was 38 cm. and his chest 33 cm. in diameter; his length was 53 cm. His eyes showed bilateral lenticular opacities that were termed "polar cataracts." The left cornea was steamy,

although the right was clear. There was increased intraocular pressure demonstrated with a tonometer, and a diagnosis of bilateral hydrophthalmos was made. Examination otherwise revealed no abnormalities, but it was impressive that the infant was well developed, with adequate subcutaneous tissue. He was admitted to the hospital for surgical procedures to relieve intraocular tension. At operation it was apparent that there were firm adhesions between the irides and the lenses. Iridencleisis on the left and an iridectomy on the right were performed.

Laboratory studies at that time revealed a red blood cell count of 3,600,000 and a white blood cell count of 11,800, with a normal differential count. Urine examination revealed a 3+ reaction for albumin and a 0 to 1+ reaction for sugar. The urine sediment contained many granular casts and crystals. The infant's course following operation was benign except for occasional temperature elevations.

At 5 months of age, the patient was seen in the outpatient department because of eczema. The examiner was impressed with the fact that the infant seemed hyperactive, and a wandering nystagmus was noted. It seemed questionable whether the patient had light perception.

A roentgen examination of the wrists at 5 months of age demonstrated normal bones. A urine examination showed albumin and casts as before, but no reaction for sugar. The specific gravity was increased on one occasion to 1.018; pH varied from 6.0 to 6.5. White blood cells and crystals were seen in the sediment. Attempts to obtain sterile urine were unsatisfactory, and cultures revealed rare Staphylococcus pyogenes var. albus and Escherichia coli. It was the impression of the attending physician at that time that in each instance these bacteria represented contamination and did not have their origin in a urinary tract infection.

One month later the patient was readmitted to the hospital because of anorexia and constipation. Physical examination demonstrated that the blood pressure was 100 mm. Hg systolic; no diastolic value was obtained. Two urine specimens obtained by catheterization revealed Staph. pyogenes var. albus. The urine contained albumin (1 to 2+), but there was no reaction for sugar or acetone; many granular crystals and occasional white blood cells were noted in the sediment. The pH on one occasion was as low as 5.5. During hospitalization the patient was intermittently febrile without an accompanying leucocytosis and with no obvious cause demonstrable on physical examination. At the time of discharge the parents were directed to give him 3 gm. of calcium lactate, 2 gm. of sodium lactate, and 1,500 I.U. of vitamin D a day. Thus, at 6 months of age, administration of moderately large doses of vitamin D and large doses of calcium and sodium salts was started.

On Nov. 28, 1947, when the child was almost one year of age, he was readmitted to the hospital for study (Fig. 1). At that time he could sit with support. Only two teeth were present. He had a piercing high-pitched scream, which he uttered frequently, usually without obvious cause. A roentgen examination of the wrists (Fig. 5, left) showed only one carpal center but no observable rickets or osteitis. An oral dextrose tolerance test produced a rise of more than 40 mg. per 100 cc. A tuberculin test (dilution, 1:1,000) gave a negative reaction, as did a Hinton test for syphilis. Urine examination gave much the same results as previously. Urine was concentrated to a specific gravity of 1.025 and diluted to 1.004. The red blood cell count, hemoglobin concentration, and white blood cell count were not remarkable. Results of studies performed at this time, including values for the electrolyte and metabolite concentrations in the blood and urine, are recorded in Tables 1 and 2.

Again it was noted that the patient was intermittently febrile. Because it seemed important to establish whether this child needed added basic salt therapy to prevent osseous abnormalities and since he had had these for the last six months without the development of rickets or osteomalacia, the added salt administration was stopped but the vitamin D therapy was continued.

On May 8, 1948, the child was readmitted to the hospital for study. At that time a roentgenogram of the forearm revealed active rickets (Fig. 5, right). The reflexes were considerably diminished, and the plantar response was normal. A psychomotor examination when the child was 17 months old demonstrated that his development was that of a 4-month-old infant. Eight teeth were present, and this was felt to be at the lower limit of normal for a patient of his age. A dental consultant thought that the teeth were well calcified and free of caries.

Again, a roentgen examination of the abdomen revealed no renal calcification. With the appearance of active rickets and the change in the serum phosphatase level, it was felt justified to reinstitute therapy. Therefore, he was discharged to be given a regimen which included 1,500 I.U. of vitamin D and added calcium lactate and sodium lactate.

PATIENT 2 (MGH 457905).—D. M. was born on Jan. 15, 1944; he was first seen at the Massachusetts Eye and Ear Infirmary on July 31, 1944, at 7 months of age, with the chief complaint of "eye trouble."

The mother and father were living and well. Neither a significant history of familial diseases nor one of consanguinity of the parents could be obtained. At the time there were no other siblings, but one child was born in 1947, who at 6 months of age was normal. The patient was the product of a normal full-term pregnancy, born by spontaneous delivery. The mother's health during pregnancy was normal. The weight at birth was 3,700 gm. The infant was formula-fed and ate well. Orange juice and vitamin D (1,500 I.U. a day in propylene glycol) were administered soon after the infant was taken home from the hospital. When the patient was 3 months of age, the mother noted that he did not seem to follow light with his eyes. It was the mother's impression that the patient had a "veil over his eyes." The family physician observed the patient for the first 10 months of life and because of increasing cloudiness of the corneae referred him to the Massachusetts General Hospital.

At the time of initial examination the patient was a listless infant in no apparent distress. His head was 41.5 cm. in diameter, and the blood pressure was 92/64 mm. Hg. The examiner noted that the sclerae seemed blue and the corneae "steamy." Palpation of the orbits elicited an impression of considerably increased intraocular tension. There were bilateral lenticular opacities; the child did not follow light, and no retinal red reflex could be obtained. The patient's pupils did not react to light.

A urine examination at that time revealed a 1 to 2+ reaction for albumin. The specific gravity was 1.014, and there were negative reactions for sugar and acetone. The sediment after catheterization revealed 7 to 10 white blood cells per field and many crystals. This specimen on culture produced Staph. pyogenes var. albus and alpha hemolytic streptococci. However, when the culture was repeated, the urine was sterile. The red blood cell count was 3,900,000 and the hemoglobin concentration 10 gm. per 100 ml.; the white blood cell count was 8,000, with a normal differential count.

A roentgen examination of the skull and of the chest revealed no abnormalities. Intravenous pyelograms were normal. A blood Hinton test gave a negative reaction, as did a tuberculin test done with old tuberculin in a dilution of 1 : 1,000. Because of obvious psychomotor retardation, an electroencephalogram was obtained; the tracing was not unusual. The child's course in the hospital was intermittently febrile without observable cause.

The patient was readmitted to the hospital for bilateral iridencleisis. At that time, when the patient was 1 year 8 months of age, it was noted for the first time that he could hold his head up without assistance. Urine examination revealed no reaction for sugar or acetone, but a 2+ reaction for albumin.

On June 4, 1945, the patient was 2 5/12 years of age. His head was 45 cm. and his chest 47 cm. in circumference; his length was 79 cm. It was noted that he had a gross wandering nystagmus. At that time he would sit alone for a few minutes and hold his head up, but he tired quickly. His musculature was noted to be hypotonic and no tendon reflexes could be elicited. Urine examination showed the continued presence of granular casts and a reaction for albumin, and upon this occasion a reaction for acetone was also noted. The white blood cell count was 6,400. A voided specimen of urine grew E. coli on culture. A catheterized urine specimen sent for culture was sterile. A roentgen examination of the abdomen revealed no renal calcification, and roentgenograms of the bones showed "undercalcification." An intravenous pyelogram was normal at that time.

On March 1, 1948, at 4 years 2 months of age, the child was readmitted to the hospital for study. Results of this study are summarized in Tables 1 and 2. All his life he had received 1,500 I.U. of vitamin D a day. Physical examination showed a blood pressure of 130/80 mm. Hg. The anterior fontanel was closed. The child was hyperactive, with continuous purposeless movements of the extremities. He was very irritable and had a high-pitched, piercing scream which he produced almost constantly without obvious cause. He was noted to salivate excessively. At that time his psychomotor development had still reached only the stage of being able to sit alone. He could not stand or walk. He had learned to repeat simple phrases from memory. The searching nystagmus was still present, as were the other eye abnormalities mentioned. His musculature was exceedingly flabby but not atrophic. There was an adequate supply of

fat on his limbs. No tendon reflexes could be elicited, and right cryptorchism was present. At that time roentgen examination of the abdomen revealed no renal calculi. A roentgenogram of the wrists showed considerable decalcification of the bones (Fig. 6). Results of urine examination were much as they had previously been. He could dilute and concentrate his urine, and at times the pH was distinctly acid. Results of an oral dextrose tolerance test were normal. A urea clearance test showed 85% of normal function.

PATIENT 3 (MGH 432873).—J. R. was born on Oct. 5, 1943. He was first seen at the Eye and Ear Infirmary of the Massachusetts General Hospital on Jan. 4, 1944, with the chief complaint of "eye trouble."

His mother was 24 years old and of Italian extraction. The age of his father was not known, but both parents were living and well. Both paternal grandparents were deaf-mutes. No history of consanguinity could be obtained.

The child was delivered, presumably after 10 months of gestation, by breech delivery with the application of forceps. The mother's health during pregnancy was not remarkable except for the appearance of a rash, the origin of which was unknown, during the first month. At birth the patient was said to have had "defective vertebrae, a heart that was shifted to the left, diaphragms that were too high, a poorly inflated lung, and cataracts in both eyes." Birth weight was 3,800 gm. The infant remained in the hospital for 37 days, part of which time he required oxygen administration and was fed by gavage, the exact reason for which was not known.

When the patient was 6 months of age, an examiner noted that the infant's head was flattened on the left and that there was a depression of the left hemithorax. He was also noted to have bilateral lenticular cataracts and hydrophthalmos. Also present were excessive lacrimation and photophobia. The lenticular opacities were described as bilateral "nuclear cortical cataracts." Note was made that the patient seemed to hear.

He was admitted to the Massachusetts Eye and Ear Infirmary for an operation designed to relieve the increased intraocular tension. Urine examination demonstrated a 4+ reaction for albumin, and a white blood cell count at that time was 11,800. A tuberculin test done with old tuberculin in a dilution of 1:1,000 gave a negative reaction.

On May 2, 1944, five months after the initial admission, the patient was brought to the outpatient department because of a respiratory infection. Results of physical examination were as they had been before, except for the fact that a searching nystagmus was now present. On June 14, 1944, a urine examination revealed positive reactions for albumin and sugar as previously described.

At one year of age the patient was obviously retarded; two lower and two upper incisors were present; he could neither sit up nor roll over, and the anterior fontanel was still patent.

At 3 years 3 months of age, on Jan. 7, 1947, the child was brought to the hospital by his mother because he cried whenever he was picked up. A history as obtained at that time disclosed that he had received no vitamin D for at least one year. The complaint had been present for weeks. His developmental history at that age revealed that he sat up at 1½ years, attempted to stand at 3 years, and at 3½ years had first begun to crawl. Physical examination showed a child who was fairly well developed but short for his age. Adequate subcutaneous tissue was present. There was prominence of the frontal region of the forehead, and the anterior fontanel was still patent. The eye abnormalities previously noted were also present. The blood pressure was 130/80 and 125/80 mm. Hg. There were no heart murmurs, and the osseous deformities of the chest had disappeared; a marked Harrison's groove was present, and obvious prominence of the costochondral junctions was noted. The deformity of the vertebrae, as reported by the attending obstetrician, could not be demonstrated. The abdomen, although slightly distended, was free of masses. No tendon reflexes could be elicited, and the child was extremely irritable and had a high-pitched, piercing scream. He was unable to talk. Roentgen examination of the bones showed them to be poorly calcified. The cortices were thin, with multiple fractures; the ends of the ribs were flared; the metaphyses of the arm bones were irregular in outline and broad with moderate cupping. The carpal centers of ossification were poorly delineated and decreased in number. These osseous abnormalities were compatible with a diagnosis of severe rickets. Roentgen examination of the abdomen revealed no calcification of the kidney but considerable gas in the intestine. A urine culture was sterile, and several

subsequent cultures revealed either no organisms or rare alpha streptococci and occasional coliform bacilli. It was felt that these organisms were contaminants. However, during the third week of hospitalization, after repeated attempts at catheterization, an E. coli infection in the urine developed. This was treated for eight days with streptomycin, resulting in sterilization of the urine. Intravenous pyelograms revealed no renal calcification and normally filling kidneys.

Urine examination revaled a 2 to 3 + reaction for albumin, a 0 to 1 + reaction for sugar, a 0 to 2+ reaction for acetone, a specific gravity that varied between 1.010 and 1.016, and a pH of 5.5 to 7.0. The sediment always contained many granular and crystalline casts. A blood Hinton examination gave negative results. Examination of the formed elements of the blood showed nothing remarkable. Several urea clearance determinations were normal. During the second month of hospitalization, before the institution of added basic salt therapy, but after vitamin D therapy had been started, new fractures occurred in the bones of the forearm (Fig. 3, upper). The alteration in the concentration of electrolytes in the serum can be appreciated by examination of Table 1. His hospital course was characterized particularly by intermittent fever without obvious cause. He was discharged while receiving added calcium and sodium salts and vitamin D. At that time there was apparently considerable healing of active rachitic lesions (see Fig. 3, lower).

Six months later, at almost 4 years of age, the patient was able to stand without support.

On Dec. 1, 1947, the child, now 4 years 2 months of age, was readmitted to the hospital. Since discharge his intake of medicaments had been desultory. His mother could give no accurate account of how much therapy he had received.

Results of physical examination were much as they had been previously. Most noteworthy was his good physical development, as demonstrated by more than adequate fat in a patient with chronic disease. He could now sit and stand alone. No tendon reflexes could be elicited; his bone age as demonstrated by roentgenogram was under 2 years. There was cupping of metaphyses of the radius and ulna, with calcification of metaphyseal ends suggesting healing rickets. A roentgen examination of the skull showed a linear fracture through the parietal bone. An oral dextrose tolerance test gave normal results, without glycosuria at a time the blood sugar was 162 mg. per 100 ml. There was still a 2 to 3 + reaction for albumin, with a 1 to 0 + reaction for sugar and a 0 to 2 + reaction for acetone. After restriction of fluid intake, the specific gravity of the urine increased to 1.025, while after an intravenous injection of dextrose and water the specific gravity fell to 1.004. The pH varied between 5.5 and 7.2 The red blood cell count at that time was 4,500,000; the hemoglobin concentration, 12 gm. per 100 ml., and the white blood cell count, 8,500, with 49% polymorphonuclear leucocytes, 43% lymphocytes, 6% monocytes, and 1% eosinophils. Several urea clearance determinations were normal, as were results of liver function tests. With the use of carmine markers, a three-day fat balance period with measured intake demonstrated that 95% of administered fat was absorbed. This was a normal result. Other metabolic studies were carried out as indicated in Table 2. He was discharged on a regimen which included an intake of 1.8 gm. of calcium lactate, 1 gm. of sodium citrate, and 2,500 I.U. of vitamin D a day.

On April 22, 1948, the patient was again observed in the hospital. A history as obtained at that time revealed that the mother spontaneously had discontinued the patient's base therapy after an indeterminate period of administration. She had continued giving him the vitamin D supplement. A roentgen examination of the long bones at that time revealed the return of active rickets (Fig. 4, upper). The patient, now 4½ years of age, had begun to walk. It was apparent that he had light perception, and, as before, no tendon reflexes could be elicited. Because of the rickets, a new regimen of basic salt therapy was prescribed. The patient was given calcium lactate, 3 gm. a day, sodium citrate, 6 gm. a day, and vitamin D, 50,000 I.U. a day. At the end of six weeks, vitamin D dosage was decreased to 1,500 I.U. a day, but administration of the salts was continued in previous dosage, and at that time it was apparent by roentgenogram that there had been marked healing of the rickets (Fig. 4, lower).

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RENAL FUNCTION STUDIES IN PEDIATRICS

I. Renal Hemodynamics in Children with Sickle Cell Anemia

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WHILE studying renal function in children we have obtained evidence of some rather unusual and heretofore unreported alterations of renal hemodynamics in patients with sickle cell anemia. Glomerular filtration rate (mannitol clearance), effective renal plasma flow (paraaminohippurate [PAH] clearance), and tubular excretory capacity for PAH were determined in eight children between the ages of 4 and 11 years with sickle cell anemia.

To our knowledge there are no reported data on these clearances (mannitol and PAH) in children with this disease. Calcagno and co-workers,[1] using the thiosulfate clearance method, found a reduction in the glomerular filtration rate in five children with sickle cell anemia. Two patients with sickle cell trait were observed to have glomerular filtration rates within normal limits. They, however, report one case of secondary anemia in which the glomerular filtration rate was in the higher limits of normal (144.5 cc. a minute per 1.73 square meters). It is interesting that the degree of anemia in this patient was severer than in any of the patients with sickle cell anemia. Evidence of renal functional abnormalities in adult patients with sickle cell anemia has been submitted by Levin and associates.[2] They found reductions in glomerular filtration (inulin clearance) and renal plasma flow (iodopyracet [diodrast®] clearance) in six patients with sickle cell disease.

Bradley and Bradley,[3] studying the effects of chronic anemia in adults (pernicious anemia, leucemia, paroxysmal nocturnal hemoglobinuria, chronic blood loss associated with hemorrhoids, and other forms), observed a reduction in the mannitol, inulin, and iodopyracet clearances and in the maximal tubular excretory capacity for

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1. Calcagno, P. L.; McLavy, J., and Kelley, T.: Glomerular Filtration Rate in Children with Sickle Cell Disease, Pediatrics **5**:127, 1950.

2. Levin, W. C.; Gregory, R., and Bennett, A.: Effect of Chronic Anemia on Renal Function as Measured by Inulin and Diodrast Clearances, J. Lab. & Clin. Med. **32**:1433, 1947.

3. Bradley, S. E., and Bradley, G. P.: Renal Function During Chronic Anemia in Man, Blood **2**:192, 1947.

TABLE 1.—*Renal Function in Children with Sickle Cell Anemia*

Date	Patient	Age, Yr.	Sex	Height, Cm.	Weight, Kg.	Surface Area, M²	Hemoglobin, Gm./100 Cc.	Hematocrit, Vol. %	Plasma Level at Midpoint Minus 2 Min.		Absolute Clearance Values/Period				Average Clearance Values/1.73 M.² of Surface Area				GFR × 100/ERPF*	GFR × 100/ERBF	GFR/Tm (PAH)	ERPF/Tm (PAH)	ERBF/Tm (PAH)	Urine Flow, Cc./Min.
									Mannitol, Mg./Cc.	PAH, Mg./Cc.	GFR, Cc./Min.	ERPF, Cc./Min.	ERBF, Cc./Min.	Tm (PAH) Mg./Min.	GFR	ERPF	ERBF	Tm (PAH)						
3/ 1/50	C. C.	5	M	107.0	16.2	0.695	7.5	25.0	0.264	0.0132	78.9	359.0	479.0		176.0	837.9	1,118.0	109.1	21.0	15.7	1.6	7.7	10.3	2.1
									0.267	0.0124	64.1	314.0	419.0											1.7
									0.220	0.268	74.0			46.7										3.0
									0.220	0.288	66.0			40.9										3.3
3/ 8/50	M. E.	10	F	132.5	23.2	0.944	7.5	28.0	0.378	0.0109	75.0	432.0	600.0		148.0	836.3	1,162.0	93.9	17.7	12.7	1.6	8.9	12.2	6.7
									0.355	0.0093	77.5	482.0	670.0											11.8
									0.373	0.390	91.0			53.5										5.6
									0.379	0.378	80.0			49.2										4.8
2/ 6/51	M. E.	11	F	135.9	24.9	0.993	8.5	26.0	0.351	0.0160	81.0	500.0	675.0		125.5	830.8	1,122.0	96.6	15.1	11.2	1.3	8.6	11.6	1.4
									0.350	0.0137	71.5	455.0	615.0											1.7
									0.410	1.080	64.0			55.5										3.7
3/10/50	A. F.	8	M	122.5	22.2	0.873	7.5	30.0	0.396	0.0063	98.1	540.0	771.0		188.1	985.1	1,405.8	143.9	19.0	13.4	1.3	6.8	9.8	5.6
									0.371	0.0071	98.0	455.0	650.0											11.5
									0.304	0.370	109.0			71.0										5.1
									0.332	0.302	75.0			74.4										5.6
5/29/50	A. F.	8	M	122.5	23.0	0.889	7.5	22.0	0.315	0.0049	108.0	606.0	777.0		190.6	1,107.6	1,421.5	167.9	17.2	13.4	1.1	6.6	8.5	3.6
									0.276	0.0055	115.5	530.0	680.0											8.7
									0.317	0.358	78.5			91.6										5.5
									0.294	0.330	88.9			80.6										6.6

4/12/50	T. T.	5	M	110.9	19.0	0.762	7.0	30.0	0.500	0.0150	100.0	488.0	698.0		219.1	1,048.7	1,500.5	100.4	20.9	14.6	2.2	10.4	14.9	1.2
									0.418	0.0132	95.7	436.0	623.0											1.7
									0.339	0.435	93.5			46.1										2.5
									0.315	0.590	97.0			42.4										2.7
8/ 9/50	T. T.	5	M	113.0	20.2	0.793	6.5	20.5	0.313	0.0114	77.0	404.0	510.0		159.7	877.5	1,105.2	104.4	18.2	14.4	1.5	8.4	10.6	1.2
									0.317	0.0125	82.1	401.0	504.0											1.3
									0.310	0.705	65.0			49.5										2.9
									0.339	0.860	69.0			46.3										3.0
5/26/50	W. S.	4	M	101.5	17.9	0.697	7.5	26.0	0.284	0.0062	92.7	405.0	547.0		215.7	911.4	1,232.6	155.2	23.7	17.4	1.4	5.9	7.9	3.0
									0.254	0.0061	99.5	330.0	447.0											5.6
									0.242	0.407	71.7			66.4										3.6
									0.225	0.395	84.0			59.0										3.5
7/31/50	W. S.	5	M	107.0	19.0	0.741	8.5	25.0	0.345	0.0063	76.5	450.0	600.0		163.6	906.1	1,328.0	167.9	16.4	12.3	1.0	5.9	7.9	8.0
									0.348	0.0065	76.2	405.0	540.0											5.0
									0.392	0.635	67.0			75.7										4.8
									0.440	0.885	61.2			68.6										4.6
7/24/50	A. S.	8	F	121.0	20.2	0.832	9.0	28.0	0.388	0.0099	90.9	670.0	930.0		198.8	1,320.8	1,832.5	129.7	15.1	10.8	1.4	10.2	14.1	1.6
									0.360	0.0094	91.5	600.0	833.0											1.6
									0.371	0.425	90.4			58.7										3.5
									0.387	0.625	100.5			66.0										4.6
2/ 5/51	A. S.	9	F	128.3	20.2	0.860	9.0	28.0	0.434	0.0141	66.6	425.0	590.0		133.8	881.6	1,223.8	87.9	15.2	10.9	1.5	10.0	13.9	1.0
									0.418	0.0130	69.0	461.0	640.0											0.9
									0.470	0.980	66.2			44.2										3.8
5/18/51	L. B.	11	F	134.6	23.4	0.950	8.0	24.0	0.400	0.0240	68.3	513.0	675.0		132.7	948.1	1,247.4	.....	14.0	10.6	...	....	....	1.7
									0.370	0.0187	58.9	470.0	618.0											0.9
									0.350	0.0158	94.0	597.0	785.0	....										1.6
5/21/51	L. B.	11	F	134.6	23.4	0.950	9.0	24.0	0.323	0.0226	88.5	614.0	808.0		140.4	1,105.2	1,455.0	102.8	12.7	9.65	1.4	10.8	14.1	2.4
									0.385	0.805	78.0			57.1										3.2
									0.400	0.844	77.0			57.1										3.4
5/29/51	M. M.	5	F	106.7	15.5	0.679	8.0	39.0	0.363	0.0137	67.0	292.0	479.0		176.6	721.6	1,184.2	103.9	24.5	14.9	1.7	6.9	11.4	3.4
									0.352	0.0109	65.2	274.0	450.0											7.7
									0.450	0.355	75.5			40.8										3.1

* Filtration fraction.

iodopyracet. The maximal tubular excretory capacity for glucose was normal in all patients with the exception of one with coexisting pernicious anemia and diabetes mellitus.

CLINICAL MATERIAL AND METHODS

All clearances with the exception of the second clearances on M. E. and A. S. were performed at a time that the patients were in crisis. Repeated clearances were performed in six patients after a period ranging from 3 days to 11 months after the initial studies. The second clearances on A. S. and M. E. were performed at a time that they were asymptomatic. Sickling of erythrocytes on routine blood smear stained with Wright's stain was observed in each case, as well as immediate sickling on wet preparation of capillary blood obtained five minutes after the application of a tourniquet.

The blood pressure and blood nonprotein nitrogen were observed to be normal in all cases at the time of the studies. It was necessary to transfuse a number of the patients soon after admission and before clearance studies were done because of the severity of the anemia. In no instance did the results obtained from patients who had been transfused vary significantly from results obtained from those who had not been tranfused. The hemoglobin concentration ranged from 7 to 9 gm. per 100 cc. and the hematocrit values from 21 to 39% immediately previous to the clearances (Table 1).

The patients were given a breakfast of toast and milk at the usual time and 500 cc. of water orally shortly before the studies were begun. An indwelling bladder catheter was inserted, and a blank urine specimen was collected. The bladder was irrigated with sterile isotonic sodium chloride solution, and complete emptying was assured by manual expression after the instillation of air. A priming dose of mannitol and paraaminohippurate was given intravenously and followed by a continuous intravenous infusion of these substances in the arm opposite the one from which blood samples were withdrawn. A 20-minute period was allowed for equilibration, which resulted in adequate and consistent blood levels. Accurately measured urine collection periods ranged between 13 and 15 minutes each. Blood samples were withdrawn at the beginning and end of each period. After two periods the concentration of paraaminohippurate (PAH) in the infusion was increased to bring the plasma level of PAH up sufficiently high to measure the maximal tubular excretory capacity for PAH (Tm_{PAH} [Table 1]). At this point a 30-minute period was allowed for equilibration, and urine and blood samples were collected for two additional periods. The load/Tm_{PAH} ratio was found to exceed 1.5 in all cases.

Mannitol in the blood and urine was determined by the method of Corcoran and Page[4] and the PAH levels by the method of Smith and co-workers.[5] The plasma levels of mannitol and PAH were plotted on semilog paper; from this graph the levels were determined corresponding to the midpoint of each urine collection period minus two minutes. No correction factor for glomerular filtration rate (GFR [comparison with inulin]) was used in the analysis of these data. The body temperature was followed, and in no instance was it necessary to make any correction for Tm_{PAH}.

In three cases it was considered necessary to discontinue the procedure after one period of Tm. measurement because of the degree of illness and/or undesirable side-effects associated with the high plasma concentrations of PAH. Effective renal blood flow (ERBF) filtration fraction (GFR/ERPF), and the ratios GFR/ERBF, GFR/Tm_{PAH}, ERPF/Tm_{PAH}, and ERBF/Tm_{PAH} were calculated and are reported in Tables 1 and 2. All values of ERPF (effective renal plasma flow), ERBF, GFR, and Tm_{PAH} referred to in the following discussion have been corrected to a body surface area of 1.73 square meters, utilizing the formula of DuBois and DuBois.[6]

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4. Corcoran, A. C., and Page, I. H.: Method for the Determination of Mannitol in Plasma and Urine, J. Biol. Chem. **170**:165, 1947.

5. Smith, H. W.; Finkelstein, N.; Aliminosa, L.; Crawford, B., and Graber, M.: Renal Clearances of Substituted Hippuric Acid Derivatives and Other Aromatic Acids in Dog and Man. J. Clin. Invest. **24**:388, 1945.

6. DuBois, D., and DuBois, E. F.: Clinical Calorimetry: Tenth Paper: Formula to Estimate the Approximate Surface Area If Height and Weight Be Known, Arch. Int. Med. **17**:862 (June) 1916.

Control clearances were performed on 11 normal children of similar ages during the time of these observations and are reported in Table 2. As a further check on our methods, all blood and urine samples collected during three separate clearances were analyzed for PAH and mannitol in two laboratories completely isolated from each other. In all cases the data obtained were in close agreement.

RESULTS AND COMMENT

Individual and summarizing data are recorded in Tables 1 and 2. Results of a statistical analysis of each measured function are recorded in Table 2 and demonstrate a significant increase in ERPF, ERBF, GFR, and Tm_{PAH}. The circulating red cell volume was increased but not significantly so. A striking increase in ERPF and ERBF was observed in practically every case whether or not the patient was in crisis. The ERPF ranged from 722 to 1,321 cc. a minute. This represents an increase of from 18.5 to 117% above the mean for normal children (Table 2). In some cases, as with normal children, rather wide fluctuations occurred during

TABLE 2.—*Comparison of Renal Hemodynamics in Children with Sickle Cell Anemia with Those in Normal Children of Similar Age*

Group		GFR, Cc./Min.*	ERPF, Cc./Min.*	ERBF, Cc./Min.*	Total Erythrocyte Flow, Cc./Min.*	Tm_{PAH}, Mg./Min.*	$\frac{GFR \times 100}{ERPF}$†	$\frac{GFR \times 100}{ERBF}$	$\frac{GFR}{Tm_{PAH}}$	$\frac{ERPF}{Tm_{PAH}}$	$\frac{ERBF}{Tm_{PAH}}$
Normal	Range	110-170	450-750	600-1,119	150-380	65-107	16.0-25.0	10.7-22.4	1.2-1.7	5.0-8.7	6.7-12.2
	Mean	128	609	866	284	90	21.0	14.3	1.4	6.8	9.9
Sickle cell anemia	Range	126-219	722-1,321	1,105-1,833	228-511	88-168	12.7-24.5	9.7-17.4	1.0-2.2	5.9-10.4	7.9-14.9
	Mean	169	958	1,309	351	120	17.7	13.0	1.4	7.9	10.9
Critical ratio ‡.....		2.93	4.68	5.61	2.32	3.18					

* Corrected to 1.73 $M.^2$ of surface area.
† Filtration fraction.
‡ Critical Ratio = difference in means/standard error of the difference;

$$\text{standard error of difference} = \sqrt{\frac{(N_1 + N_2) \cdot (\Sigma d^2_1 + \Sigma d^2_2)}{N_1 \cdot N_2 \,[(N_1 - 1) + (N_2 - 1)]}}$$

in which N_1 is the number of determinations on normal children, N_2 is the number of determinations on patients with sickle cell anemia, Σd^2_1 the sum of the squared deviations in the normal group, and Σd^2_2 the sum of the squared deviations in the sickle cell group.

the periods of individual clearances and probably are related to changes in the general systemic circulation.[7] Also, variations occurred between the first and second clearances, especially in the case of A. S. The ERBF ranged from 1,105 cc. a minute, which is within the upper limit of normal, to as high as 1,833 cc. a minute, which is from 24 to 105% above the mean for normal children of similar ages and is substantially higher than the average value for normal adults reported by Bradley and Bradley.[3] It is also considerably higher than the value which can be calculated from Rubin and Rapoport's data on children, using their plasma flow and hematocrit values.[7]

An attempt may be made to explain the increased renal plasma flow and increased blood flow on the basis of (*a*) anemia with its associated cardiovascular

7. Rubin, M. I.; Bruck, E., and Rapoport, M.: Maturation of Renal Function in Childhood: Clearance Studies, J. Clin. Invest. **28**:1144, 1949.

adjustments, (*b*) renal circulatory alterations secondary to anoxia,[8] and (*c*) possible juxtamedullary bypass [9] within the kidney, the existence of which is now doubted.[10]

Although the works of Wintrobe [11] and Sharpey-Schafer [12] indicate that among the adjustments of the circulatory system to anemia are increased cardiac output and decreased circulation time and peripheral resistance, Bradley and Bradley [3] have shown that in many forms of chronic anemia blood may be diverted from the kidney to other organs more susceptible to hypoxia. The increments in ERPF and ERBF reported here would not permit us to conclude that such is the case in children with sickle cell anemia, since the kidneys of these patients have avidly shared in the increased peripheral blood flow associated with the anemia (Tables 1 and 2). It appears from a calculation of the total erythrocyte volume (mean ERBF a minute minus mean ERPF a minute) which circulates through the kidney every minute in these patients with sickle cell anemia that even though the hematocrit and hemoglobin values are low, the increase in ERBF tends to minimize renal anoxia. The mean total erythrocyte volume circulating through the kidney was 283.3 cc. a minute in normal children and ranged from 228 to 511 cc. a minute in children with sickle cell anemia. The efficiency of this mechanism is naturally dependent upon the ability of the erythrocytes of these patients to accept, transport, and release oxygen.

The GFR was definitely increased, ranging from normal to 219 cc. a minute which is 71% above the mean for normal children (Tables 1 and 2). In 50% of the clearances values were obtained which exceeded the upper limit of normal. In spite of the increase in GFR, further reference to Tables 1 and 2 reveals that the filtration fraction and the GFR/ERBF ratio were usually reduced. The reduction in filtration fraction (in both clearances on A. S., L. B., and M. E. and in one clearance on A. F., W. S., and T. T.) indicates that the amount of glomerular filtrate formed relative to the quantity of plasma available for filtration is less than normal, although the GFR is higher than normal. This may be interpreted to mean that the reabsorptive load (water, electrolytes, or other) on the tubular cells is less than it would be if the filtration fraction were normal with such a high ERPF. It is apparent that the increase in ERPF with a proportionally smaller increase in GFR results in the formation of a sufficient quantity of filtrate to minimize the possibility of the development of azotemia. Whether alteration in filtration pressure or glomerular capillary permeability or actual glomerular damage is responsible for the reduced filtration fraction cannot be ascertained. That the total glomerular

8. Stickney, J. C.; Northrup, D. W., and Van Liere, E. J.: Effect of Anoxic Anoxia on Urine Secretion in Anesthetized Dogs, Am. J. Physiol. **147**:616, 1946. McDonald, R. K., and Kelley, V. C.: Effects of Altitude Anoxia on Renal Function, ibid. **154**:193, 1948.

9. Trueta, J., and others: Studies of the Renal Circulation, Springfield, Ill., Charles C Thomas, Publisher, 1947.

10. Maxwell, M. H.; Breed, E. S., and Smith, H. W.: Significance of the Renal Juxtamedullary Circulation in Man, Am. J. Med. **9**:216, 1950.

11. Wintrobe, M. M.: Cardiovascular System in Anemia, with Note on Particular Abnormalities in Sickle Cell Anemia, Blood **1**:121, 1946.

12. Sharpey-Schafer, E. P.: Cardiac Output in Severe Anaemia, Clin. Sc. **5**:125, 1944.

function is closely correlated with tubular excretory capacity for PAH is indicated by the fact that the GFR/Tm_{PAH} in these patients is the same as in normal children (Table 2).

The tubular excretory capacity, Tm_{PAH}, ranged from 88 to 168 mg. a minute. When compared to the mean normal value of 90 mg. a minute, this represents a maximum increase of 87% (Table 2). Results obtained during individual periods in each clearance are in close agreement (Table 1); in no instance did we obtain values significantly below the mean for normal children (Tables 1 and 2). Since Tm_{PAH} measures the maximal tubular excretory capacity for PAH, and since Tm_{PAH} is increased, there appears to be an increase in the functioning tubular tissue. The fact that ERPF/Tm_{PAH} and ERBF/Tm_{PAH} tend to be higher in children with sickle cell anemia than in normal children (Tables 1 and 2) suggests that there is a disproportionate increase in vascularity and/or vasodilatation. The possible role of anoxia in producing these alterations in renal function should again be emphasized. Alving and co-workers,[13] using simulated high altitude exposure to produce repeated periods of anoxia in human subjects, observed that the tubular functioning mass as measured by Tm. for iodopyracet was increased and remained so for weeks to months. This observation may possibly be correlated with the increase in Tm_{PAH} observed by us, because of the possible interrelationship of anemia and anoxia in our patients; however, they observed no significant alteration in glomerular filtration or renal plasma flow.

SUMMARY

Renal hemodynamics using mannitol and paraaminohippurate clearances have been measured in eight children between the ages of 4 and 11 years with sickle cell anemia.

GFR, ERPF, ERBF, and Tm_{PAH} were significantly increased.

The filtration fraction and the ratio GFR/ERBF were usually reduced, indicating a proportionally greater increase in ERPF and ERBF, the significance of which is discussed.

The ratio GFR/Tm_{PAH} is practically the same as in normal children.

The ratios ERPF/Tm_{PAH} and ERBF/Tm_{PAH} were usually greater than normal.

The possible influence of anemia, anoxia, and renal circulatory alterations have been mentioned.

Dr. C. R. Houck, Associate Professor of Physiology, University of Tennessee College of Medicine, gave advice and council relative to the experimental procedures reported in this paper, and Miss Dorothy Fair conducted control analyses during the course of this study.

13. Alving, A. S.; Adams, W.; Bay, E. B.; Bryan, A. H.; Carmichael, H. T.; Case, T.; Halstead, W. C.; Landowne, M., and Ricketts, H. T.: The Effects of Chronic Intermittent Anoxia in Man: IV. Studies of Renal Function, National Research Council, Division of Medical Sciences, Committee on Aviation Medicine Report No. 135, 1943.

DIARRHEA OF THE NEWBORN

Report of Epidemic and Results of Treatment with Streptomycin

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AND
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NUMEROUS reports of epidemic diarrhea of the newborn have been made since its recognition as a new disease in 1937 by Rice, Best, Frant, and Abramson.[1] The specific etiology has not been established in the majority of epidemics. Similarly, the exact mode of transmission is not known. However, poor hygienic care of the newborn is recognized as an important contributory factor in the spread of the disease, since most epidemics have occurred in crowded, understaffed nurseries.

We wish to report an epidemic of diarrhea which occurred in the newborn nursery of Freedmen's Hospital. A preliminary abstracted report was published previously.[2] The epidemic began in mid-August and terminated early in September of 1946. It occurred during a period when an increased number of obstetrical deliveries imposed a serious burden on hospital facilities. The nurseries were overcrowded, and there was a critical shortage of nursing personnel.

REPORT OF AN EPIDEMIC

Incubation Period.—Assuming that inoculation occurred on the first day in the nursery, the average incubation period was 4.6 days. Age at onset of disease ranged from 2 to 14 days.

Symptoms.—Diarrhea was the first symptom noted in 50 of the 53 cases. Characteristically, the stools were frequent, explosive, watery, and yellow or yellow-green. They frequently contained mucus, rarely gross blood, and never pus.

Other common symptoms were subnormal temperature, dehydration, apathy, weak swallowing reflex, anorexia, and vomiting. Hyperpnea was common in the severely dehydrated patients and could be correlated with chemical evidence of acidosis. Jaundice, although frequently noted, could not readily be distinguished from ordinary physiologic icterus. Convulsions occurred in four cases and indicated

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Dr. Brown was formerly a resident in Pediatrics; he is now residing in Baltimore.

From the Department of Pediatrics, Howard University College of Medicine, and the Pediatric Service of Freedmen's Hospital.

1. Rice, J. L.; Best, W. H.; Frant, S., and Abramson, H.: Epidemic Diarrhea of the Newborn, J. A. M. A. **109**:475 (Aug. 14) 1937.

2. Scott, R. B.: Epidemic of Diarrhea in the Newborn, Proc. Am. Federation Clin. Res. (1946) **3**:73, 1947.

a poor prognosis. Head jerking or abrupt extension of the head synchronous with respiration was usually a terminal phenomenon. Sclerema occurred terminally in seven cases.

Pathology.—Eleven cases came to autopsy. The only uniform finding was a gastroenteritis evidenced by hyperemia of the mucosa and characterized histologically by a cellular infiltrate consisting predominately of mononuclears with a varying concentration of polymorphonuclears. No gross ulcerations of the gastrointestinal tract were observed.

Pulmonary involvement consisting of engorgement, edema, or pneumonitis was present in seven cases. The frequency of pulmonary complications has been noted by other observers.[3]

Laboratory Studies.—Hemoglobin values were high early in the disease owing to dehydration and plethora of the newborn, but later decidedly low values were encountered. Plasma proteins were consistently low, averaging 4.5 gm. per 100 cc. Carbon-dioxide-combining power determinations were usually low, averaging 27.7 vol. %. All blood cultures were sterile.

Stool cultures revealed Escherichia coli, Micrococcus pyogenes var. albus, Bacillus subtilis, and Streptococcus faecalis. Salmonella enteritidis was isolated in seven cases, but in five of these it was present only at autopsy. The same organism was found in the stool of one of the nursery personnel. Antibodies for Salmonella could not be demonstrated in the blood of the two infants from whom the organism was isolated during life. No virus studies were done.

Clinical Course.—Six days to one month were required for recovery from the disease, with a median of approximately two weeks. Seven apparently cured patients were readmitted once with a relapse of the disease, and one patient, twice. Deaths usually occurred during the second or third week of the disease.

Morbidity and Mortality.—Morbidity and mortality rates for the series are given in the following tabulation:

Total number of live births	227	Gross morbidity rate	23%
Full-term infants	209	Gross mortality rate	9.2%
Premature infants	18	Case fatality rate	39%
Total number of diarrhea cases	53	Full-term infants	35%
Full-term infants	42	Premature infants	54%
Premature infants	11		
Total deaths	21		
Full-term infants	15		
Premature infants	6		

Treatment.—Symptomatic and supportive measures were employed, including isolation, sulfonamides, penicilllin, and infusion of blood, plasma, and electrolyte solutions.

Streptomycin was given to 11 patients in daily doses of 0.5 gm. intramuscularly and 0.5 gm. orally in divided doses at three-hour intervals for 10 days.

Streptomycin had no effect on the number or character of the stools but did exert a definite, albeit transitory, effect on the bacteriologic content of the stool (Table). It will be noted that stool cultures became sterile at some time during therapy in nine cases. However, in five cases organisms appeared in the stools

3. Greenberg, M., and Wronker, B. M.: Outbreak of Epidemic Diarrhea in the New-Born, J. A. M. A. **110**:563 (Feb. 19) 1938. Barenberg, L. H.; Levy, W., and Grand, M. J. H.: Epidemic of Infectious Diarrhea in the New-Born, ibid. **106**:1256 (April 11) 1936.

during therapy after an initial suppressive effect had been noted. All stool cultures contained the usual enteric organisms 48 hours after therapy was discontinued. S. enteritidis was isolated from three of the streptomycin-treated patients, all of whom died. In one of these infants the organism was demonstrated only before treatment, and in the others, only at autopsy.

COMMENT

Clifford [4] classified reported epidemics of neonatal diarrhea according to etiology as follows: (1) bacterial infection, (2) virus causation proved or suspected, and (3) no inciting agent demonstrated.

Effect of Streptomycin on Bacteriologic Content of Stools

Case No.	Duration of Diarrhea Before Treatment, Days	Outcome	Stool Cultures				
			Before Treatment	During Treatment		48 Hr. After Treatment Discontinued	Autopsy
				2d Day	8th-10th Day		
1	14	Recovered	E. coli; M. pyogenes var. albus; B. subtilis; Str. faecalis	Sterile	Sterile	E. coli; B. subtilis	.....
2	12	Died 9th day	E. coli; M. pyogenes var. albus; Str. faecalis	Sterile	.....	.....	S. enteritidis
3	11	Died 2d day	E. coli; Str. faecalis; S. enteritidis	.....	.....	.....	Candida albicans
4	12	Died 8th day	E. coli; Candida albicans; Str. faecalis; A. aerogenes	.....	.....	.....	S. enteritidis
5	17	Recovered	.....	Sterile	E. coli; Str. faecalis	E. coli; M. pyogenes var. aureus; B. subtilis	.....
6	13	Died 2d day	.....	Sterile	.....	.....	.....
7	18	Recovered	.....	.....	E. coli	E. coli; M. pyogenes var. albus; B. subtilis	.....
8	3	Recovered	.....	Sterile	E. coli; Str. faecalis	.....	.....
9	12	Recovered	.....	Sterile	E. coli	Str. faecalis	.....
10	12	Recovered	.....	Sterile	E. coli	E. coli; B. subtilis	.....
11	16	Recovered	.....	.....	Sterile	E. coli; B. subtilis	.....

Most bacterial epidemics are caused by adult carriers or are part of a generalized epidemic in the community. Organisms which have been implicated include M. pyogenes var. aureus, Pseudomonas aeruginosa, hemolytic E. coli, Streptococcus, and Salmonella.[5]

4. Clifford, S. H.: Diarrhea of the Newborn, New England J. Med. **237**:969 (Dec. 25) 1947.

5. Ensign, P. R., and Hunter, C. A.: Epidemic of Diarrhea in Newborn Nursery Caused by Milk-Borne Epidemic in Community, J. Pediat. **29**:620 (Nov.) 1946. Wegman, M. E.: Epidemic of Diarrhea Among Breast-Fed Newborn Infants, J. A. M. A. **145**:962 (March 31) 1951. Abramson, H.; Frant, S., and Oldenbusch, C.: Salmonella Infection of the Newborn: Its Differentiation from Epidemic Diarrhea and Other Primary Enteric Disorders of Newborn, M. Clin. North America **23**:591 (May) 1939. Rubenstein, A. D., and Britten, S. A.: Epidemic Diarrhea of Infancy, J. Pediat. **38**:457 (April) 1951. Epstein, H. C.; Hochwald, A., and Asche, R.: Salmonella Infections of the Newborn Infant, ibid. **38**:723 (June) 1951. Clifford.[4]

Virus etiology has ben established in very few epidemics. Light and Hodes [6] in four epidemics involving newborn nurseries were able to reproduce a similar disease in calves by intranasal inoculation of stool filtrates. In an epidemic of stomatitis and diarrhea not limited to newborn infants, Buddingh and Dodd [7] isolated a filtrable agent which would produce lesions on the cornea of rabbits.

In the majority of reported epidemics the clinical picture has presented the following characteristics: the disease has been limited to newborn infants; the chief symptom was diarrhea; the major pathogens were absent from the stools, and virus studies, if done, failed to reveal a transmissible filtrable agent.[8] Most of these epidemics have occurred in overcrowded nurseries where breaks in nursing technic were inevitable.

Our epidemic seems to fit into the last category as regards epidemiology, symptomatology, pathology, and absence of bacterial pathogens. The significance of the finding of Salmonella organisms in seven cases is not clear. Failure to demonstrate the organism in the majority of cases excludes it as the main cause of the epidemic. These cases may represent a small secondary epidemic due to an adult carrier.

Streptomycin has been used with varying results in enteric infections of older infants. Good results have been reported in Salmonella infections.[9] In nonspecific diarrhea of infants past the newborn period, reported results have ranged from dramatic to ineffective.[10]

We have been able to find only one report of the use of streptomycin in epidemic diarrhea of the newborn. Mitchell [8a] reported an epidemic very similar to ours in which neither bacterial nor viral pathogens could be demonstrated. He treated six patients with streptomycin and noted no effect upon the course of the disease.

In our small series of patients treated with streptomycin no beneficial effects were observed; four of the 11 streptomycin-treated infants died between the second and ninth days of therapy. Those who recovered showed no amelioration of their clinical course which could be attributed to the drug. Dosages were approximately the same for each unit of body weight as those recommended by Pulaski and Amspacher [9b] for the treatment of nonspecific diarrhea of infants.

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6. Light, J. S., and Hodes, J. L.: Studies on Epidemic Diarrhea of New-Born: Isolation of a Filterable Agent Causing Diarrhea in Calves, Am. J. Pub. Health **33**:1451 (Dec.) 1943.

7. Buddingh, G. J., and Dodd, K.: Stomatitis and Diarrhea of Infants Caused by Hitherto Unrecognized Virus, J. Pediat. **25**:105 (Aug.) 1944.

8. (*a*) Mitchell, E. E., and others: Neonatal Diarrhoea: Report of an Epidemic and Attempts at Isolation of a Causal Agent, Clin. Proc. **7**:251 (Aug.) 1948. (*b*) Footnotes 1 and 3.

9. (*a*) Ross, S.; Burke, F. G.; Rice, E. C.; Bischoff, H., and Washington, J. A.: Streptomycin in the Treatment of Salmonella Enteritis in Infants, New England J. Med. **240**:602 (April 14) 1949. (*b*) Pulaski, E. J., and Amspacher, W. H.: Streptomycin Therapy for Certain Infections of Intestinal Origin, ibid. **237**:419 (Sept. 18) 1947.

10. Holzel, A.; Martyn, G., and Apter, L.: Streptomycin Treatment of Infantile Diarrhoea and Vomiting, Brit. M. J. **2**:454 (Aug. 27) 1949. Leisti, P.: Treatment of Infantile Diarrhoea by Streptomycin, Ann. med. int. Fenniae **36**:575, 1947. Loeschke, A., and Cochlovius, A.: Action of Streptomycin in Dyspepsia and Toxicosis, Arch. Kinderh. **136**:154, 1949. Goettsch, E.; Cobley, G., and Mulloy, M.: Treatment of Infantile Diarrhea with Streptomycin and an Oral Amigen Mixture, Pediatrics **2**:1 (July) 1948. Aguirre, A.; Aguayo, A. S., and Benavidez, L.: Results Obtained with Streptomycin Therapy of Eight Cases of Diarrhea with Escherichia Coli or Proteus, Rev. españ. pediat. **5**:551 (July-Aug.) 1949. Pulaski and Amspacher.[9b]

The observed transient bacteriostatic effect of streptomycin upon the stool flora is interesting, but streptomycin cannot be considered of any practical value in the treatment of epidemic nonbacterial diarrhea in the newborn because of failure to alter the course of the disease.

SUMMARY

An epidemic of nonbacterial diarrhea in a newborn nursery is reported. Eleven patients were treated with streptomycin orally and intramuscularly, and this had no apparent effect upon the course of the disease.

Dr. Robert P. Crawford, Cleveland, formerly resident in Pediatrics, assisted in collection of data presented in this report. Dr. Ruth Moore of the Department of Bacteriology and Dr. Robert Jason of the Department of Pathology also gave valuable help in this study.

Case Reports

EHLERS-DANLOS SYNDROME

Report of a Case with Suggestion of a Possible Causal Mechanism

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THE SYNDROME of hyperelastic skin associated with orthopedic abnormalities has been described many times, and there are readily available summaries of the literature written both before the description of this syndrome by Ehlers and Danlos [1] and more recently.[2] The purpose of the present paper is to suggest a possible relationship between hyperadrenocorticism and this disease.

While hyperelasticity of the skin (dermatochalasis), extreme flexibility of the joints (arthrochalasis), and the formation of pseudotumors and subcutaneous nodules are usual features of the completely devleoped Ehlers-Danlos syndrome, it is commonly agreed that one of the most striking manifestations is extreme fragility of the skin (dermatorrhexis).[3] Moreover, not only is the fragility of the skin outstanding, but also the great difficulty these patients experience in healing even the smallest cuts and bruises. There is a marked absence or delay of fibrous tissue formation, so that eventually the wound is covered by epithelium, giving rise to the fragile, papyrus-like scars described by various authors.[4]

The abnormality of the subepithelial structure is emphasized by recent histological studies. In many of the older reports the sections were reported as showing an overabundance of elastic fibers,[5] although some found no such promi-

From the Department of Pediatrics and the Division of Laboratories, The Jewish Sanitarium and Hospital for Chronic Diseases.

1. Burrows, A.: Epidermolysis Bullosa with Cutis Hyperelastica, Proc. Roy. Soc. Med. **25**:1319, 1932.

2. (*a*) Smith, C. H.: Dermatorrhexis (Ehlers-Danlos Syndrome), J. Pediat. **14**:632, 1939. (*b*) Benjamin, B., and Weiner, H.: Syndrome of Cutaneous Fragility and Hyperelasticity and Articular Hyperlaxity, Am. J. Dis. Child. **65**:247 (Feb.) 1943. (*c*) Johnson, S. A. M., and Falls, H. F.: Ehlers-Danlos Syndrome: Clinical and Genetic Study, Arch. Dermat. & Syph. **60**:82 (July) 1949. (*d*) Freeman, J. T.: Ehlers-Danlos Syndrome, Am. J. Dis. Child. **79**:1049 (June) 1950.

3. (*a*) Pittinos, G. E.; Ehlers-Danlos Syndrome with a Disturbance of Creatine Metabolism, J. Pediat. **19**:85, 1941. (*b*) Ronchese, F.: Dermatorrhexis, with Dermatochalasis and Arthrochalasis (So-Called Ehlers-Danlos Syndrome), Am. J. Dis. Child. **51**:1403 (June) 1936. (*c*) Tobias, N.: Danlos Syndrome Associated with Congenital Lipomatosis, Arch. Dermat. & Syph. **30**:540 (Oct.) 1934.

4. (*a*) Footnote 2*a*, *c*, and *d*. (*b*) Albright, F., and Reifenstein, E. C.: Parathyroid Glands and Metabolic Bone Disease, Baltimore, Williams & Wilkins Company, 1948, p. 165.

5. (*a*) Smith.[2a] (*b*) Freeman.[2d] (*c*) Footnote 3. (*d*) Albright and Reifenstein.[4b] (*e*) Barber, H. S.; Fiddes, J., and Benians, T. H. C.: The Syndrome of Ehlers-Danlos, Brit. J. Dermat. **53**:97, 1941. (*f*) Stillians, A. W., and Zakon, S. J.: Cutis Laxa (Cutis Hyperelastica), Arch. Dermat. & Syph. **35**:342 (Feb.) 1937. (*g*) Navarro Martín, A., and Aguilera Maruri, C.: Un caso de cutis laxa y lesions atróficas de tipo eritromiélico, Actas dermo-sif. **25**:126, 1932. (*h*) Miget, A.: Le syndrome d'Ehlers-Danlos, Thesis, Paris, Louis Arnette, 1933. (*i*) Weber, F. P.: Chalasodermia or "Loose Skin" and Its Relationship to Subcutaneous Fibrous or Calcareous Nodules, Urol. & Cutan. Rev. **27**:407, 1923.

nence of the elastic tissue.[6] On the other hand, more recent histological studies have indicated that the basic pathological changes may be in the collagen sbstance.[7]

In addition to the striking abnormalities of the cutis and subcutis, these patients often exhibit a remarkable fragility of the blood vessels, so that even gentle handling may result in marked ecchymosis and purpura.[8] Some authors, in trying to explain the vascular fragility, found a low ascorbic acid content of the blood, with increased retention of the vitamin after administration of a test dose.[9]

The symptoms referable to the skin and blood vessels of patients with Ehlers-Danlos syndrome seem to bear considerable resemblance to the findings in patients suffering from Cushing's syndrome or receiving prolonged treatment with corticotropin (ACTH). It is generally known that corticotropin and cortisone exert profound effects on the collagen system. Retardation of healing in patients with Cushing's syndrome has been reported by Cope, who in recent years has operated on most of these patients at the Massachusetts General Hospital, Boston.[10] It is also well established that there is a failure of, or a delay in, the granulation of wounds suffered by patients under treatment with corticotropin or cortisone. This has been reported in human subjects and has been experimentally demonstrated in rabbits.[11] Moreover, Ragan and associates, impressed by the fragility of the blood vessels, with consequent tendency to bruising and ecchymosis, were able to demonstrate a low blood ascorbic acid and a decreased urinary excretion of vitamin C in both human and animal subjects who were receiving prolonged treatment with corticotropin.

The patient whose case history follows was studied with these facts in mind.

REPORT OF CASE

P. G., a 4½-year-old white boy, was admitted to the hospital because of hypermobility of all the joints since birth, together with the recent onset of weakness. His father, 42 years old, and a cousin were known to be "double-jointed." The mother was 31 years of age and well. There was no consanguinity. There were no siblings. The pregnancy was uneventful; the labor was "dry" and lasted 48 hours. Delivery was spontaneous after gestation of eight months. There was no cyanosis or convulsions.

Hypermobility of all his joints and elasticity of the skin were noted at birth. Dislocation of the hip was noted early, and several futile attempts were made at reduction and maintenance of position with plaster.

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6. Williams, A. W.: Cutis Laxa, Monatsschr. prakt. Dermat. **14**:490, 1892. Pautrier, M.: Note histologique sur un cas de cutis elastica, avec pseudotumeurs aux génaux et aux caudes, prèsenté par M. Danlos, Bull. Soc. franç. dermat. et syph. **19**:72, 1908. Brown, A., and Stock, V. F.: Dermatorrhexis: Report of a Case, Am. J. Dis. Child. **54**:956 (Oct.) 1937.

7. Smith.[2a] Tobias.[3c] Footnote 5*g* and *i*. Footnote 6. Ormsby, O. S., and Tobin, W. W.: Cutis Hyperelastica, Arch. Dermat. & Syph. **38**:828 (Nov.) 1938. Burrows, A., and Turnbull, H. M.: Cutis Hyperelastica (Ehlers-Danlos Syndrome), Brit. J. Dermat. **50**:648, 1938. Bolam, M.: A Case of Ehlers-Danlos Syndrome, ibid. **50**:174, 1938.

8. Johnson and Falls.[2c] Tobias.[3c]

9. Benjamin and Weiner.[2b] Pittinos.[3a] Albright and Reifenstein.[4b]

10. Cope, O., cited by W. Bauer, in discussion on Loeb, R. F.: Clinical Studies with Cortisone and ACTH, in Adrenal Cortex: Transactions of the First Conference, Nov. 21-22, 1949, edited by E. P. Ralli, New York, Josiah Macy, Jr., Foundation, 1950, p. 121.

11. Ragan, C.; Howes, E. L.; Plotz, C. M.; Meyer, K., and Blunt, J. M.: Effect of Cortisone on Production of Granulation Tissue in the Rabbit, Proc. Soc. Exper. Biol. & Med. **72**:718, 1949.

The boy on admission was well developed, intelligent, and cooperative. He was active, although confined to bed. In the rehabilitation clinic he cooperated well and was intelligent. Physical examination revealed dermatorrhexis, dermatochalasis, and arthrochalasis. The skin of any part of his body could be extended 3 to 4 inches (7.6 to 10 cm.) as shown in Figure 1, and snapped back promptly when released. There were a few papyrus-like scars, and the skin also had the soft, "pleasant" feel which has often been described.[2a,d] The dermatorrhexis was especially evident when venepuncture was attempted; the skin cracked in five to six radiating lines, like a piece of tissue paper touched by a wet finger. There was no skin or subcutaneous resistance to the needle point during penetration. Even mild handling produced bruising and ecchymosis, and every attempt to do a venepuncture resulted in huge extravasations of blood. There were no skin tumors or subcutaneous nodules.

The general looseness and hypermotility of all the joints were striking. The fingers could be extended to almost twice their length, and many joints could be rotated at will in any

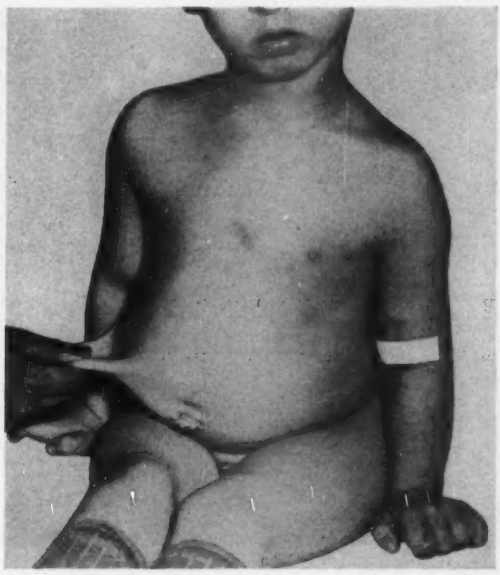

Fig. 1.—Excessive elasticity of the skin and ecchymosis after venepuncture.

direction (Fig. 2). The head of the right femur could be easily felt lying in the acetabulum. On the left side the hip could be dislocated at will. Both knees went into the recurvatum position but did not subluxate. The ankles were always either in extreme eversion or in extreme inversion. He had the muscle power to move each joint voluntarily and was able to perform practically full range of motion against gravity. Pes cavus was present. There was deformity of the metatarsal ends of the phalanges. He was able to sit up himself, and he walked when supported, though on the inner borders of his feet.

The head was 20 inches (50.8 cm.) in circumference; it seemed larger because of the prominent frontal bosses. The sutures and fontanels were closed. The eyes were normal, but there was a definite blueness to the sclerae. The heart and lungs were normal. The pulse rate was 108; the blood pressure was 102 mm. Hg systolic, and 80 mm. diastolic. The spleen and liver were normal. The teeth were normal.

Roentgenologic examinations, aside from those already noted, showed a marked disproportion of the facial bones and moderate but definite osteoporosis of the metacarpal and forearm

bones (Fig. 2), of the spine, and of the elbow. Roentgenograms of both the wrists and the elbows (Fig. 2) showed definite retardation of epiphyseal development. The roentgenograms also demonstrated the extreme arthrochalasis.

Chemical analysis of the blood revealed the following values: glucose, 114 mg.; urea nitrogen, 16.1 mg.; uric acid, 3.3 mg.; calcium, 9.4 mg.; phosphorus, 5.8 mg., and total proteins, 6.83 gm. (globulin, 3.64 gm.; albumin, 3.19 mg.), per 100 cc. Sodium was 143 mEq. and potassium 4.76 mEq. per liter. Cholesterol measured 216 mg. and total lipids 810 mg. per 100 cc. Two tests of the dextrose tolerance with 30 gm. of dextrose given by mouth, and one test with 8.5 gm. given intravenously, showed normal curves. Results of repeated examinations of the urine were normal. The 24-hour urinary excretion of sodium was 153.0 mEq. per liter, and that of potassium, 102 mEq. The 17-ketosteroid content in three separate 24-hour urine specimens determined in two separate laboratories was 3.94 mg., 2.5 mg., and 2.9 mg. The amount of oxyketosteroids in a similar specimen was 0.65 mg. (This determination was performed in the laboratory of Dr. Louis Soffer. By Dr. Soffer's method, this value is within

Fig. 2.—Roentgenogram of elbow joint, demonstrating extreme flexibility of the joint, retarded epiphyseal development, and osteoporosis.

normal limits.) The uric acid-creatinine ratio in a 24-hour specimen of urine was 1.82. After the intravenous injection of 1,000 mg. of ascorbic acid, 770 mg. was excreted within five hours.

Hematological examinations revealed the following: Hemoglobin concentration varied between 11.5 and 12.5 gm. per 100 cc.; red blood cells numbered 3,980,000 to 4,130,000, and white blood cells 8,200 to 14,200 per cubic millimeter, with 54 to 58% polymorphonuclear cells, 38 to 41% lymphocytes, 1 to 4% mononuclear cells, and 2% eosinophiles. Bleeding time was 4 minutes and coagulation time 5.5 minutes. Thrombocytes (platelets) were normal. A bone marrow specimen showed "moderate lymphocytic infiltration and erythroblastosis; normal myeloid and megakaryocyte elements." The circulating eosinophiles were 78 per cubic millimeter.

COMMENT

The data presented in this paper certainly do not prove that the Ehlers-Danlos syndrome is caused by a disturbance of the pituitary or the adrenal cortex. They do not even prove that the basic etiological factor attacks the endocrine system as well as the other mesodermal structures. However, we can point out several points

of similarity between this syndrome and the syndrome of prolonged hyperadrenocorticism. The table lists the pertinent symptoms and laboratory findings in Cushing's syndrome, in patients receiving corticotropin or cortisone, in our patient, and in reported cases of Ehlers-Danlos syndrome.

According to normal values recorded by Talbot and associates,[12] by Read and his co-workers,[13] and more recently by Kenigsberg and colleagues,[14] the excretion of 17-ketosteroids by our patient was definitely elevated, and this indicates increased activity of the adrenal cortex.[15] While the eosinophile count is not a reliable index of adrenal cortical activity,[14] the value of 78 cells per cubic centimeter in our patient is lower than that reported as normal.[16]

Symptoms and Laboratory Findings in Cushing's Syndrome, in Patients under Treatment with Corticotropin or Cortisone, in Reported Cases of Ehlers-Danlos Syndrome, and in the Present Case

Symptom or Laboratory Finding	Cushing's Syndrome	Corticotropin or Cortisone Treatment	Reported Cases of Ehlers-Danlos Syndrome	Present Case
Dermatorrhexis	+	+	+	+
Delayed healing	+	+	+	+
Fragile blood vessels	+	+	+	+
Weakness	+	..	+	+
Acrocyanosis	+	+	+	0
Osteoporosis	+	+	Mentioned once	+
Delayed epiphyseal development	+	+	Not reported	+
Obesity	+	+	Occasionally	0
Hypertension	+	+ or −	0	0
Striae	+	+	0	0
Acne	+	+	0	0
Abnormal dextrose tolerance curve	+	+ or −	Not reported	0
Increase of 17-ketosteroids in urine	+	+	Not reported	+ or −
Increase of oxycorticoids in urine	+	+	Not reported	0
Increase of uric acid-creatinine ratio	+	+	Not reported	+
Increased ascorbic acid retention	+	+	+	0
High blood sodium	+ or −	+ or −	Not reported	0
Low blood potassium	+ or −	+ or −	Not reported	0
Lymphocyte count	Low	Initial depression; later, increase	No consistent findings	Normal
Polymorphonuclear count	Increased	Increased	Nothing consistent	Normal
Eosinopenia	+	+	None reported	+ or −

There were some symptoms of hyperadrenocorticism which were not found in our patient or in reported cases of Ehlers-Danlos syndrome. The most important

12. Talbot, N. B.; Butler, A. M.; Berman, R. A.; Rodriguez, P. M., and MacLachlan, E. A.: Excretion of 17-Keto Steroids by Normal and Abnormal Children, Am. J. Dis. Child. **65**:364 (March) 1943.

13. Read, C. H.; Venning, E. H., and Ripstein, M. P.: Adrenal Cortical Function in Newly-Born Infants, J. Clin. Endocrinol. **10**:845, 1950.

14. Kenigsberg, S. P.; McGavack, T. H., and Pearson, A.: The Excretion of 17-Ketosteroids: Normal Values in Relation to Age and Sex, J. Clin. Endocrinol. **9**:426, 1949.

15. Read and others.[13] Kenigsberg and others.[14]

16. Venning, E. H.: The Effect of ACTH During the Neo-Natal Period, in Proceedings of First Clinical ACTH Conference, edited by J. R. Mote, Philadelphia, The Blakiston Company, 1950, p. 25. Hills, A. G.; Forsham, P. H., and Finch, C. A.: Changes in Circulating Leukocytes Induced by the Administration of Pituitary Adrenocorticotrophic Hormone (ACTH) in Man, Blood **3**:755, 1948.

discrepancy is the normal value we found for oxysteroids. However, it is generally accepted that not all symptoms described as indicating overactivity of the adrenal cortex appear in Cushing's syndrome or in patients treated with corticotropin or cortisone. According to Soffer,[17] the development of alterations in glucose metabolism does not occur uniformly in cases of cortical hyperfunction. In Bunim's series [18] only 3 of 18 patients treated with corticotropin displayed glycosuria. In the same series only two patients gave evidence of potassium depletion. Soffer [19] reported that less than half the patients with adrenal cortical hyperfunction exhibit some abnormality in the blood electrolytes.

As noted, our patient was one month premature. A surprising number of reported cases contain the same history.[20] We do not understand the relationship of this fact to the possible glandular disturbance.

SUMMARY

A typical case of Ehlers-Danlos syndrome is presented. This patient had the following symptoms, signs, and laboratory findings which may also be observed in patients with adrenal hyperadrenocorticism: (*a*) dermatorrhexis; (*b*) poor fibroblast response to subcutaneous injury; (*c*) fragile blood vessels; (*d*) weakness; (*e*) osteoporosis; (*f*) delayed epiphyseal development; (*g*) high normal or slightly increased excretion of 17-ketosteroids in the urine; (*h*) increase of the uric acid to creatinine ratio in the blood, and (*i*) eosinopenia.

80 Linden Blvd.

17. Soffer, L. J.: Clinical and Experimental Studies on Adrenal Cortical Hyperfunction, Bull. New York Acad. Med. **24**:32, 1948.

18. Bunim, J. J.: The Clinical Effects of Cortisone and ACTH on Rheumatic Diseases, Bull. New York Acad. Med. **27**:75, 1951.

19. Soffer.[17] Soffer, L. J.: Clinical Manifestations of Adrenal Cortical Hyperfunction, Bull. New York Acad. Med. **23**:479, 1947.

20. Footnote *2a* to *c*. Footnote 3.

Progress in Pediatrics

EARLY DESCRIPTIONS OF CONGENITAL PYLORIC STENOSIS

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THE PROBLEM of who was the first to describe congenital pyloric stenosis is an exercise in diagnosis, as well as in historical research, which crops up from time to time. It has not hitherto been settled, and Major's "Classic Descriptions of Disease" [1] contains no note on pyloric stenosis. The publication of Prof. Arvid Wallgren's Abraham Flexner lectures [2] provides an opportunity for sorting the tares from the wheat. Wallgren states that the muscular hypertrophy of the pyloric sphincter remains for many years after the symptoms have disappeared, operation or no, and this may have a bearing on one of the earliest recorded cases. Wallgren also states that the first recorded description was by Hirschsprung (in 1888). This, however, cannot be accepted. It is proposed here to give extracts from several early descriptions which have from time to time been championed by eminent authorities.

HILDANUS, 1646

Kellett [3] quotes Hildanus' case of "a six months old child, the eldest son of Henry Otho, Esq." The onset of vomiting was several days before. The child recovered, and there was no postmortem examination.

This is a very doubtful case indeed and would nowadays be classed as one of a feeding difficulty—for, as Hildanus wrote, "The child's stomach had been for several days crammed by his nurse or mother with a thick and viscid pultaceous feed. . . ."

BLAIR, 1717

Blair [4] reported on a child who

> . . . seem'd to be healthy till he was about a Month old, when he was seized with a violent Vomiting, and a Stoppage of Urine and Stool. Some time after, both these became more regular, but the Vomiting still continued. He seem'd to have a great Appetite, taking what Suck, Drink, or other Food was offer'd him, with a kind of eagerness; but he immediately threw it all up again.

He died at 5 months of age, and postmortem study showed that he

> . . . was so emaciated, that he appear'd rather to have decreased, than to have encreased in Bulk, from the time of his Birth; his whole Body not weighing above five Pounds. The Skin and Muscles of the Abdomen were very thin, but the Peritoneum was preternaturally thick. The

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1. Major, R. H.: Classic Descriptions of Disease, Springfield, Ill., Charles C Thomas, Publisher, 1932.

2. Wallgren, A. J.: Tuberculosis and Other Problems of Pediatrics, Baltimore, Williams & Wilkins Company, 1950.

3. Kellett, C. E.: Arch. Dis. Childhood **8**:323, 1933.

4. Blair, P.: Phil. Tr. Roy. Soc., London, 1717, No. 353, p. 631.

Ventriculus was more like to an Intestin than to a Stomach, its length being five Inches, and its breadth but one Inch. The coats of it were thick and fleshy, and the Cavity very inconsiderable. The Pylorus, and almost half of the Duodenum were cartilaginous, and something inclin'd to an Ossification, so that no Nourishment could have passed into the Intestins, tho' the Stomach had been capable of containing it, which makes it no wonder that the Body was so emaciated. There were scarce any footsteps of the Omentum to be seen, even at the Bottom of the Stomach, to which it usually adheres.

The right Lobe of the Lungs adhered firmly to the Ribs and had three Exulcerations, which contain'd purulent Matter. It was so very thin and compact, that it seem'd as if that Lobe had never been of use in Respiration. The left Lobe was of a more florid Red, spongy, and free from any Adhesion.

Sir Frederic Still [5] calls this the earliest description at present known, and Parsons and Barling [6] consider it the earliest case.

One is loath to disagree with such eminent authorities, but there are several doubtful features here: first, the sudden onset: ". . . he was seized with a violent Vomiting"; second, ". . . a Stoppage of Urine," which is unusual but may have been due to reduced fluid intake; third, the postmortem finding that the stomach was abnormally small, its coats fleshy, and the cavity inconsiderable; in pyloric stenosis the stomach is, it is true, sometimes hypertrophied but it is always dilated as well, and fourth, the fact that "the Pylorus and almost half of the Duodenum were cartilaginous"; the thickening in pyloric stenosis stops short at the entrance into the duodenum.

Possibly the bulging of the pylorus into the duodenum misled Dr. Blair.

On the whole, it seems possible that this may have been a true case, that the child had pyloric stenosis from which it was recovering, but died from secondary infection—of the lungs and possibly of the peritoneum also. The pyloric tumor remained, and also the hypertrophy of the stomach wall, though the dilatation had abated.

However, it has so many doubtful features that it cannot stand indisputably as the first typical case.

CALDER, 1733

Calder [7] wrote of "Two Examples of Children born with preternatural Conformations of the Guts." The first was a case of exomphalos. The second was as follows:

. . . I visited another Child, which lived full seven Days after the Birth, in which time it had never voided any *Fæces per anum*, but vomited everything it swallowed; which did not appear to have any mixture of *Meconium*, Bile, or any other coloured Substance.

The Parents, who were both healthy and sound, having formerly lost several Children with the same Symptoms, desired me to examine the Body of this Child, to discover the Cause of their Death.

The Stomach was in good Condition, but the *Pylorus* was very hard, and felt as if it contained some other Substance, which appeared upon opening of this inferior Orifice of the Stomach, to be a glandular-like Piece of solid Flesh, so closely adhering to the *Pylorus* all round, that there was no separating of it, and without the least Perforation in it any where; so

5. Still, G. F.: The History of Paediatrics: The Progress of the Study of Diseases of Children up to the End of the XVIIIth Century, London, Oxford University Press, 1931.

6. Parsons, L. G., and Barling, S. G.: Diseases of Infancy and Childhood, London, Oxford University Press, 1933.

7. Calder, J., in Medical Essays and Observations, Revised and Published by a Society in Edinburgh, Ed. 3, Edinburgh, Ruddimans, 1733, Vol. 1. p. 164.

that the Passage was quite shut up. Below this, the *Duodenum* was divided into two; and the Gut continued thus divided to about one third of an Inch above the *Jejunum*. Into the largest of these *Intestinula* the biliary Duct opened.

All the Intestine below were distended with Air, and only a small quantity of *Meconium* was to be seen near the *Podex*.

The other *Viscera* were all sound.

This case has several features suggestive of pyloric stenosis, especially the family history and the description of the tumor. However, many other features are against it: the early death (at 7 days) and the complete absence of feces and an opening in the pylorus.

This seems to be a case of duodenal atresia. It is interesting to compare this with Cautley's account of duodenal stenosis.[8]

. . . the prolongation of life for more than a few days . . . is an extremely rare event. . . . A dilated first part of the duodenum gives the sensation of a pyloric tumour, but it is neither so hard nor so well defined . . . the common duct may divide into two branches, one of which may open into the stomach or even into the large intestine.

It seems possible that Calder's patient had several strictures, that the double duodenum was really a duodenum with a block and a bile duct bypass. Perhaps one may surmise from his description of the tumor that hypertrophic pyloric stenosis was present as well, and that this is what the other children died of. However, this again is not a typical case.

WEBER, 1758

Christopher Weber[9] in his inaugural dissertation for the degree of Doctor of Medicine at the University of Göttingen made "Some Observations upon Diseased Bodies of Infants."[9] His third observation, "Mors ex spasmo pylori," contains the following, as quoted in English by Still.[5]

A newly born female child sucked milk without difficulty but soon after she had filled her stomach with this infant-nourishment she returned it by vomiting; she died on the sixth day after birth.

The postmortem examination showed the following features:

The pylorus was hard to the touch like cartilage, and contracted. On incision, its substance was seen to be thick, and the tightness of its contraction made the lumen similar. It must be supposed therefore that in the child during life the pylorus was in such spasm that it passed none of the stomach contents into the duodenum, but the stomach rejected them all by vomiting, but owing to the relaxation of the spasm by death, the contracted lumen was patent. What was noted in the intestines too proves that the pyloric opening was entirely closed before death. There was no trace whatever of chyme or digested food but the duodenum was full of fluid bile like that found in the gallbladder, and although the bile extended up to the pylorus, not the smallest drop of it had passed into the stomach.

This case cannot be accepted, as the child died too early, and no digested food was found in the intestine. Congenital pyloric stenosis does not cause symptoms from birth, and the spasm is not severe enough to prevent all food from passing through.

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8. Cautley, E.: Brit. J. Child. Dis. **16**:65, 1919.

9. Weber, C.: Some Observations upon Diseased Bodies of Infants, Inaug. Diss., Göttingen, 1758; cited by Still.[5]

However, Weber continues, after citing Calder's cases which have been mentioned above:

I have also observed some of these same points in another child, a boy of ten weeks old; I could not however ascertain of what disease he died: I found the pylorus contracted and hard, the bowels empty of chyme, but full of air and blown up, and in many parts contracted and pale except where the gallbladder was in contact with them; there were very scanty small pieces of stool scattered in the coecum and colon.

This reads more like a genuine case. "A boy of ten weeks old" and "scanty small pieces of stool" are suggestive. Though the details given are not all that we should like, there are no anomalous features.

ARMSTRONG, 1771

Armstrong's report [10] was as follows:

In a child about three weeks old that died of the watery-gripes some time since, and which I opened, I found most of the stomach, towards the upper orifice, and almost the whole fundus, in the same tender state with that of the child just now mentioned [i. e., upon handling the stomach gently he found the coats of it gave way as if they had been reduced by maceration to almost a gelatinous consistency]. But towards the *pylorus*, the structure was firm enough, as likewise that of the intestines, both small and great. The stomach was quite distended with curdled milk and victuals, with which the nurse had crammed the child, mixed likewise with some of the chalk julep, but the whole intestines were remarkably empty. There was no morbid appearances [*sic*] to be observed any where but in the stomach; and this *viscus* being so full, while the intestines were almost empty, it looked as if the disease had been chiefly owing to a spasm in the *pylorus*, which prevented the contents of the stomach from passing into the *duodenum*. Perhaps cases of this kind are more frequent than is commonly imagined. . . . This is the third child . . . which the parents have lost at the same age, and in the same disease.

This is generally accepted as a true case and is the first to be described by a British physician.

BEARDSLEY, 1788

Sir William Osler [11] considered Beardsley's [12] description to be the first, and he reprinted the whole note, of which the following is an extract:

A child . . . in the first week of its infancy, was attacked with a puking, or ejection of the milk, and of every other substance it received into its stomach almost instantaneously, and very little changed. The feces were in small quantity and of an ash color, which continued with little variation till its death. . . . Aliment taken in small quantities would often remain on it [the stomach], till, by the addition of fresh quantities, the whole, or nearly all, was ejected. . . . In this situation, with very little variation of symptoms he continued till death closed the painful and melancholy scene, when he was about five years of age.

Postmortem examination made on the second day after death showed that

. . . the esophagus was . . . greatly distended [and] between the circular fibres which compose the middle coat, were small vesicles, some of which contained a tablespoonful of a thin fluidlike water. . . . [The stomach] coats were about the thickness of a hog's bladder when fresh and distended with air. . . . The pylorus was invested with a hard compact substance, or schirrosity, which so completely obstructed the passage into the duodenum, as to admit with the greatest

10. Armstrong, G.: An Essay of the Diseases Most Fatal to Infants, Ed. 2, London, T. Caddell, 1771.

11. Osler, W.: Arch. Pediat. **20**:355, 1903.

12. Beardsley, H., in Cases and Observations by the Medical Society of New Haven County in the State of Connecticut, New Haven, J. Meigs, 1788, pp. 81-84.

difficulty the finest fluid. . . . The vesica fellis, which was nearly five inches in length and more than one in diameter . . . lay transversely across the abdomen, and was bedded into the small intestines, which were sphacelated [gangrenous] wherever they came in contact with it; its contents were rather solid than fluid, and resembled flesh in a highly putrid state; its color was that of a very dark green. . . . The necessity there was of interring the body that evening, put a stop to any further examination.

For some time it seemed that this could not be admitted as a case because of the prolongation of life to 5 years; but Wallgren's report of the persistence of the tumors for several years alters the possibilities. The description of the vomiting is suggestive; but the ashen color of the feces is not. No mention is made of jaundice in the patient.

It seems that there was some obstruction of the bile duct and of the pylorus also; possibly this was a case of multiple congenital defects.

So, on the whole, it seems that Weber's second case was the earliest on record.

Caulfield [13] notes the anomalies in Blair's description but says, ". . . The balance of the description is so strikingly typical that it admits of little doubt of the identity of the disease." He adds: "One cannot expect to find a twentieth century description of the disease; his [Blair's] unfamiliarity with the picture may account for some of the unusual features."

This may be so, but if we accept an author's description we must accept it *in toto* and not reject those parts which do not fit in with our own particular theories. Moreover, "unfamiliarity with the picture" did not prevent Addison, Bright, Graves, and others from describing most accurately and beautifully diseases which have since become known by their names.

13. Caulfield, E.: Early Case of Pyloric Stenosis, Am. J. Dis. Child. **40**:1069 (Nov.) 1930.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

A Clinical Study Concerning the Value of Biolac. Sprague Hazard and Clement A. Smith, J. Pediat. **38**:18 (Jan.) 1951.

Biolac® has been improved. Coconut oil and destearinated beef fat have been substituted for the original fat. About 60% of the lactose content has been replaced by a maltose-dextrin combination. This new biolac® appears to be a satisfactory food for promoting proper growth in young infants.

Macdonald, Pittsburgh.

On the Use of Mare's Milk in Infant Feeding. H. Kalliala, E. Seleste, and N. Hallman, Acta pædiat. **40**:94 (March) 1951.

The properties of mare's milk and its suitability for infant feeding have been investigated.

The chemical composition of mare's milk is similar to that of human milk. It is also an albumin milk. The fat content is, however, much lower, and the mineral content is somewhat higher, this applying especially to the calcium and phosphorus. The keeping property of the mare's milk received at the hospital, as defined by the reductase test, is poorer than that of first-class human and cow's milk. The bacterial flora does not seem to be different from cow's milk. The souring seems to proceed in the same way in all these milks. The lysozyme content seems to be very low.

In vitro experiments showed that the digestibility of mare's milk is practically the same as that of human milk, i. e., considerably better than that of cow's milk. In healthy children, even 75 to 85 Cal. per kilogram a day (mare's milk has 410 Cal. per liter; human and cow's milk, 700 Cal.) was in many cases enough to produce a good increase in weight. If the food consists of mare's milk only, it ought to be given in amounts of 210 to 220 cc. per kilogram of body weight. Other ways would be to add a quantity of cream and sugar to the mare's milk or to give a part of the ration as citric acid milk.

The stools during mare's milk feeding are definitely alkaline, approximately similar to stools during cow's milk feeding. The character of the fecal flora is between that of cow's milk and that of human milk stools. The urine is relatively slightly acid. Mare's milk seems to be quite suitable for the early stages of treatment of infantile diarrhea.

From the Authors' Summary.

Vitamins; Avitaminoses

Absorption of Ascorbic Acid During Simultaneous Administration of Cod Liver Oil or Concentrate of Vitamins A and D: Clinical and Experimental Investigations. Erling Rustung, Nord. med. **37**:533 (March 12) 1948.

Load tests with ascorbic acid or ascorbic acid in addition to different kinds of vitamin D compounds were made on healthy children. The object of these investigations was to find out whether the absorption of the ascorbic acid was enhanced by cod liver oil or by any one of its constituents. It is concluded that in respect to absorption of ascorbic acid, no antagonistic effect of practical importance was demonstrated by cod liver oil or by the vitamins A or D_2.

Wallgren, Stockholm, Sweden.

Pellagra in a Child. Sigleif Dalaker, Nord. med. **38**:695 (April 2) 1948.

A 5-year-old girl had from the age of 3 years been receiving a deficient diet which had consisted principally of carbohydrates. She displayed anorexia, increasing muscular weakness, symmetrical photosensitive dermatitis, cheilitis, extreme emaciation and inertia, tremor, anxiety, and greatly reduced mental ability. With large doses of nicotinic acid, given orally and by

injection, a rapid improvement of the dermatological and neurological symptoms occurred, while the mental improvement was slower.

WALLGREN, Stockholm, Sweden.

Prematurity and Congenital Deformities

UNILATERAL MACROSTOMIA: CASE REPORT. ROBERT H. CLIFFORD, Ann. Surg. **130**:1098 (Dec.) 1949.

Clifford reports this case of macrostomia because of the rarity of the condition. Only five cases have been reported in Europe since 1881. No cases have been reported in America. The method of surgical treatment is given in detail.

BANTIN, Omaha.

SOME VIRUS DISEASES DURING PREGNANCY AND THEIR EFFECT ON THE FETUS. HERMAN GRÖNVALL and PER SELANDER, Nord. med. **37**:409 (Feb. 27) 1948.

Among 27 cases of German measles in women during pregnancy there were three missed abortions and one malformation (fifth month). Among 20 cases of measles there were three missed abortions, no malformations. Among 13 of varicella there was one missed abortion. Among 34 of epidemic parotitis there were one missed abortion and five malformations (one in the first, two in the fifth, one in the sixth, and one in the eighth month). Among 29 cases of epidemic hepatitis there were four missed abortions and one malformation (in the third month). Among 38 of poliomyelitis there were 11 missed abortions and two malformations (in the third and eighth months). One of the two women with herpes zoster had missed abortion. In 13 cases of scarlet fever there were no missed abortions, no malformations.

Among 354 mothers of malformed children, rubella occurred four, possibly five, times; measles once, varicella once, epidemic parotitis five times, hepatitis at least three times, and poliomyelitis at least twice. The calculated frequency of virus diseases during pregnancy in women in general is 0.47%; the frequency in mothers of defective children was about 5%. Virus diseases were thus found to occur 10 times oftener in mothers of malformed children than in pregnant women in general attending lying-in hospitals.

WALLGREN, Stockholm, Sweden.

Newborn

GREEN TEETH FOLLOWING ICTERUS NEONATORUM. CHARLES PINCKNEY, Proc. Roy. Soc. Med. **42**:561 (July) 1949.

The patient, a girl of 11 months, showed eight teeth, all of which showed a bluish-green pigmentation. The lower central incisors erupted at 5 months. Jaundice was noticed at birth. The color rapidly deepened during the first week. There was considerable enlargement of liver and spleen at birth. The urine contained bile pigment, and the red cell count was only 2,900,000, with 18 nucleated red cells per 100 leucocytes. The icterus index was 180. Three transfusions of group O, Rh-negative blood were required in the first week. The jaundice had cleared by 3½ months. At admission to the hospital the patient had a red blood count of 4,840,000 and 86% hemoglobin. The blood types of the other members of the family were father, group O, Rh positive; mother, group A, Rh negative; and a baby, group A, Rh positive.

WILLIAMSON, New Orleans.

HEPATIC CIRRHOSIS WITH NONHEMOLYTIC ICTERUS IN THE NEWBORN. M. NEGRI, Minerva pediat. **2**:565 (Dec.) 1950.

A fatal case of congenital cirrhosis of the liver in a 2-month-old baby is reported. An autopsy was performed. The etiology of the condition is obscure. The salient findings were malnutrition, icterus, hepatosplenomegaly, a faintly positive direct and a strongly positive indirect van den Bergh reaction, absence of biliary pigment in the urine, a negative Wassermann reaction, hyperchromic anemia with macrocytosis, serological compatibility (Rh) with the mother, and death from bronchopneumonia.

This type of prehepatic nonhemolytic jaundice, while seen in adults, is uncommon in the newborn; the cirrhosis appears to be primary and due to toxins which passed through the placental barrier.

HIGGINS, Boston.

CASE OF WINCKEL'S DISEASE. M. SAGGESE, Pediatria **59**:117 (Jan.) 1951.

On the fourth day of life a girl began to vomit bloody material and to pass dark feces. By the seventh day she was markedly jaundiced and cyanotic. The liver and spleen were enlarged. Spectroscopic examination of the blood gave the lines of methemoglobin. Treatment was by penicillin, oxygen, vitamin K, and transfusions. The blood of the mother and of the child were of the same groups. The child died two weeks after the onset of symptoms, with disseminated bronchopneumonia and enteritis. The autopsy report recorded icterus, degeneration of the liver parenchyma, bronchopneumonia with subpleural petechiae, and a catarrhal enteritis. The diagnosis of Winckel's disease (AM. J. DIS. CHILD. **60**:1375, 1940) was made. The importance of the methemoglobinemia as of etiological significance is stressed.

HIGGINS, Boston.

OBSERVATIONS ON TREATMENT OF MORBUS HEMOLYTICUS WITH EXCHANGE TRANSFUSIONS OR TRANSFUSIONS. HAINZ KÖLBL, Wien. klin. Wchnschr. **63**:307 (April 27) 1951.

The indications for transfusion and for exchange transfusion are discussed, as well as the techniques of exchange transfusion, on cases of icterus gravis. Special attention is paid to the justification of nursing. The antibody titer of the mother of an infant with icterus gravis was strangely positive. The colostrum also had a high titer. In this case the electrophoretic determination of the colostrum proteins showed a pronounced increase of the alpha and beta globulins. Milk taken a fortnight later, while the antibody titer of the mother's serum remained high, had lost the Rh antibodies, and the electrophoretic serum protein analysis had become normal. It is concluded that neither an Rh nor an A-B-O incompatibility between mother and child constitutes a contraindication to nursing.

AMBERG, Rochester, Minn.

TREATMENT IN A CASE OF TETANUS NEONATORUM ACCORDING TO THE METHOD OF SPERANSKY. E. MARTISCHNIG and O. THALHAMMER, Wien. klin. Wchnschr. **63**:353 (May 11) 1951.

Eight days after birth an infant was taken ill with trismus; on the 16th day generalized tonic spasms began. The infant received repeated injections, intramuscular and intravenous, of tetanus antitoxin, and in addition spinal fluid was aspirated in a syringe and reinjected, according to the method of Speransky, with final removal of a few milliliters of fluid at each of the two sessions. This procedure was regarded as of definite benefit. The infant recovered.

AMBERG, Rochester, Minn.

EPIDEMIC DIARRHEA OF THE NEWBORN. R. GOSTOF, F. GALLIA, and J. SVABENSKA, Paediat. danub. **6**:187 (Oct.-Dec.) 1949.

Three outbreaks of epidemic diarrhea of the newborn occurred in different places of Bohemia in the spring of 1949. Two were observed in maternity wards, one in a premature unit. The mortality was 25% and 40% in mature infants, 66% in premature infants. The clinical picture of the disease showed nothing exceptional. Noteworthy was the contemporaneous occurrence of herpes in the mothers. Bacteriological search for the causative agent brought no explanation. Virological tests were performed at the decline of every outbreak, so that only a few patients were tested. The results, however, enabled the authors to conclude that the causative agent was a virus.

FROM THE AUTHORS' SUMMARY.

IMMUNITY IN THE NEWBORN. J. SCHUBERT and A. GRÜNBERG, Pediat. listy **5**:100 (No. 2) 1950.

The authors summarize briefly the modern aspects of the problem of antibody production in the newborn and report that in 34 newborn infants vaccinated against typhoid agglutinins were produced. The antibody titers are not in direct proportion to the weight or stage of development of the baby and attain on the average one-half to one-fourth of the value which is common in adults under the same experimental conditions. The appearance of agglutinins in infants after vaccination is similar to that in adults, but the titer seems to diminish quicker. The colostrum of the newborn contains only traces of agglutinins.

The result of this work—together with the findings of other authors working with different categories of antibodies—shows the necessity of revising the obsolete view that the newborn baby is incapable of producing antibodies.

FROM THE AUTHORS' SUMMARY.

CLINICAL ASPECTS OF ERYTHROBLASTOSIS FETALIS. ARNE NJÅ, Tidsskr. norske lægefor. **68**:237 (May 15) 1948.

Njå reports 38 patients with erythroblastosis fetalis, of whom seven died. Kernicterus was supposed to be the cause of death in five cases, cerebral hemorrhage in one case, and no definite cause of death was found in the seventh case. Of the 31 surviving children, two showed mental retardation and one was atactic; the others were healthy.

WALLGREN, Stockholm, Sweden.

Acute Contagious Diseases

POLIOMYELITIS IN THE EARLY NEONATAL PERIOD: REPORT OF A CASE OF POSSIBLE INTRAUTERINE INFECTION. ALEXIS SHELOKOV and LOUIS WEINSTEIN, J. Pediat. **38**:80 (Jan) 1951.

An infant was born in a tank respirator of a mother dying with fulminating poliomyelitis. Poliomyelitis developed on the sixth day of life. At the age of 1 year he had marked paralysis of the right leg and weakness of the muscles of the left leg.

MACDONALD, Pittsburgh.

EFFICACY OF IMMUNIZATION AGAINST DIPHTHERIA. MANUEL BLANCO OTERO, Acta pediat. españ. **90**:669 (June) 1950.

Dr. Otero, of the Health Department in Madrid, is answering an article by Dr. Rendu which appeared in the *Acta Pediatrica Española*, No. 82, 1949, and certain other articles which appeared in the French journals. He gives figures on mortality and morbidity of diphtheria as collected by the department from 1901 to 1948 and shows the actual number of cases and the percentage for every 100,000 inhabitants during these years. The actual number of cases in 1901 was 4,729, or 25.1%, while in 1948 the number was 263, or 0.9%. He also shows that the greatest decline has occurred since children under one year of age have had immunization. Otero cites figures from other countries as well. He also mentions the study made by Foley of the Canadian Public Health Association on children immunized and children not immunized. In unprotected children the morbidity was 136 per 10,000 inhabitants and the mortality 19.2%. In protected children there were no deaths and only 1.8% morbidity. Otero also states his belief that most of the medical world agrees with him as to the value of immunization.

ALLEN, Santa Fe, N. M.

SMALLPOX VACCINATION AND COMPLICATIONS OBSERVED IN THE FIRST MONTH OF THE MASSIVE VACCINATION CAMPAIGN (1950). DARIO SEPULVEDA R., Acta pediat. españ. **98**:127 (Feb.) 1951.

The author gives statistics of complications which arose in Santiago, Chile, during the first month of a mass vaccination program. The program was undertaken because several cases of smallpox were discovered in the country and two in Santiago. There had been no mass program since 1944, but many persons had been protected by various health agencies and their private physicians during this interval.

During the first month the author took care of 400 children who had complications and were brought into the hospital or outpatient department. Classified, the complications ranged from local necrosis to encephalitis. The author discusses the theories of the causation of encephalitis. He feels that diagnosis of eczema and similar skin and allergic conditions should be carefully made. Pediatricians and maternal health centers should be responsible for the vaccination of infants. Infants should be protected against smallpox, preferably in the second trimester of life, since it is then that they have the least natural immunity; there is also less danger of complications at that time.

ALLEN, Santa Fe, N. M.

TREATMENT OF SCARLET FEVER WITH PENICILLIN (PROCAINE). JOSE MARIA ABAD GARCIA, Acta pediat. españ. **98**:152 (Feb.) 1951.

This is a study of 100 patients with scarlet fever to whom penicillin procaine was administered intramuscularly for six days. The dose was 200,000 units daily. All patients were ambulatory, and a follow-up study was made on each daily for six weeks.

Before treatment 69% showed a growth of hemolytic Streptococcus in throat cultures. After 24 hours of treatment only 3% showed positive cultures, and after completion of treatment only 1.5% showed the organism in throat cultures. The results show that the bacteriological effect of penicillin procaine is as good as that of the ordinary penicillin given at more frequent intervals. There were no complications such as mastoiditis and nephritis, and none of the patients had any ill effects from the use of penicillin.

ALLEN, Santa Fe, N. M.

TREATMENT OF SCARLET FEVER WITH PENICILLIN. FRITZ LASCH, Med. Klin. **45**:1082 (Sept. 1) 1950.

The paper is based on the observation of 270 cases of scarlet fever, of which 136 were cases in which penicillin could not be administered and 134 cases in which it was given. The patients were of both sexes and all ages. The good results of others with penicillin were confirmed. Myocardial changes and focal nephritis occurred with equal frequency in the two groups. An immunity to scarlet fever does not follow shortly after a given penicillin treatment. To avoid recurrence of scarlet fever and infection of other members of a family on the return home of the patient, it is important to obtain several negative cultures from the throat for hemolytic Streptococcus.

AMBERG, Rochester, Minn.

ENUCLEATION OF THE TONSILS OF DIPHTHERIA CARRIERS. WERNER SCHMIDT, Med. Klin. **46**:548 (May 4) 1951.

Tonsillectomy, and in some adenectomy also, was done in 12 children 4 to 13 years of age and in six men, all of them chronic carriers of diphtheria bacillus. All became free of diphtheria bacilli in seven days and remained so for the control period of two years. Four of these patients had been treated with roentgen rays with transitory success.

AMBERG, Rochester, Minn.

EARLY TREATMENT OF POLIOMYELITIS SEQUELAE. W. JOSENHANS, Med. Klin. **46**:596 (May 18) 1951.

It is recognized today that the treatment of choice in cases of paralytic poliomyelitis is indefatigable massage and exercise combined with electric and hydrotherapeutic measures extending over a prolonged period. The author stresses the point that in the long run it is on the whole less expensive to restore a patient so that he can help himself than to provide care for a helpless cripple.

AMBERG, Rochester, Minn.

POLYNEURITIS FOLLOWING CUTANEOUS DIPHTHERIA AND OTHER SKIN INFECTIONS. H. STROTZKA, Wien. klin. Wchnschr. **61**:394 (June 24) 1949.

Strotzka reports on nine cases of severe polyneuritis, in several of which the condition followed proved cutaneous diphtheria; in others the disease was strongly suspected, while in the rest the neuritis was due to other suppurative lesions of the skin. From a review of the cases it is concluded that paralysis of accommodation is characteristic of diphtheritic polyneuritis, while paralysis of the palate occurs usually if there was a pharyngeal localization of the infection.

MASON, New York [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

EXPERIMENTAL INOCULATION OF ROSEOLA INFANTUM. BO HELLSTROM and BO VAHLQUIST, Acta pædiat. **40**:189 (May) 1951.

In 14 cases attempts were made to transfer the infecting agent of exanthema subitum (roseola infantum) through intramuscular injection of blood from patients with typical disease in the exanthematous stage.

Three of the patients revealed a typical symptom complex, with pyrexia beginning on the sixth to the ninth day, followed by a fall in the temperature on the 9th to the 12th day with a simultaneous exanthem. Blood changes occurred with neutropenia and relative lymphocytosis. The results suggest that an infectious agent circulates in the blood in exanthema subitum.

FROM THE AUTHORS' SUMMARY.

Acute Infectious Diseases

ACUTE GLOMERULONEPHRITIS: IMPETIGO AS AN ETIOLOGICAL FACTOR. G. C. MCCULLOUGH, J. Y. COFFEE, and P. A. TRICE JR., J. Pediat. **38**:346 (March) 1951.

In this series of 124 cases of acute glomerulonephritis, impetigo was the antecedent infection in 33% and acute tonsillitis in 31%. A miscellaneous group of acute infections accounted for the remainder. The authors suggest that since acute tonsillitis is usually treated vigorously with antibiotics, while impetigo often may be untreated, the latter disease has become more deadly by default.

MACDONALD, Pittsburgh.

RADIOLOGIC DIAGNOSIS OF URINARY TRACT TUMORS IN INFANTS AND CHILDREN. MEREDITH F. CAMPBELL, Radiology **54**:646 (May) 1950.

Roentgenographic illustrations of hydronephrosis, reduplication of renal segments, embryonal carcinoma of the kidney (Wilms's tumor), cyst, polycystic disease, adrenal sympathicoblastoma, leiomyosarcoma of the bladder, ureterocele, and fibrosarcoma of the prostate are supplied by the author. While routine urography suggests the diagnosis in most cases, thorough cystourethroscopic study is advised before surgical treatment is undertaken. For tumors, retrograde study is better than excretory pyelography.

ANSPACH, Chicago.

WILMS' TUMOR: EVALUATION OF TREATMENT METHODS. ROLFE M. HARVEY, Radiology **54**:689 (May) 1950.

A review of a large series of cases of embryonal carcinoma of the kidney (Wilms's tumor) by the author leads to the following conclusions: 1. Surgery alone is not adequate to control the tumor. 2. Irradiation has been proved to control some tumors for at least 10 years, although it is not adequate in most cases. 3. Postoperative irradiation appears to have been conclusively proved of value. 4. Irradiation has probably not been given sufficient opportunity to demonstrate its effectiveness in operable cases of this disease.

ANSPACH, Chicago.

ACUTE NEPHRITIS IN JERUSALEM CHILDREN. E. RABINOVICH and S. T. WINTER, Ann. Pædiat. **175**:396 (Nov.) 1950.

Seventy-one cases, including two recurrences, of acute nephritis in children over a period of 11 years are reported. The seasonal incidence corresponded with the Jerusalem scarlet fever incidence. The sex distribution did not show any proneness of boys to this disease, nor was sect (European or Oriental) a significant factor.

Associated infections in this series were not predominantly "deep" in type. Cardiac involvement was noted in very few cases, though this may have been due to the paucity of roentgenologic electrocardiographic investigations. The degree of nephritis was noted as mild in 41% of the series, moderate in 53%, and severe in 6%. Progress was noted as good in 60% and slow in 36%.

One child died in the hospital. Another died two months after discharge. A third child recovered from acute renal failure only after surgical decapsulation. One child was discharged who was progressing to a chronic condition. Two children were readmitted with acute nephritis after intervals of four months and six years respectively. The other children were discharged as improved or recovered, none showing signs of serious residual renal involvement.

Relaxation of the dietary regimen had no adverse effect on the clinical progress. In general, the clinical picture of acute glomerulonephritis in Jewish children in Jerusalem resembles that recorded elsewhere.

FROM THE AUTHORS' SUMMARY.

IRON CONTENT OF THE BLOOD SERUM OF CHILDREN WITH KIDNEY LESIONS. M. LATO, Clin. pediat. **32**:610 (Nov.) 1950.

The blood serum iron content in six children with acute hemorrhagic nephritis and hypochromic anemia was found to be normal, and in two children in uremic coma it was markedly elevated.

HIGGINS, Boston.

FOREIGN BODIES IN THE VAGINA OF CHILDREN. R. DANA, Pediat. listy **5**:143 (No. 3) 1950.

Foreign bodies in the vagina of children may be introduced (1) by masturbation, either by the child herself or by any other child; (2) involuntarily, by small pieces of linen or small foreign bodies in cases in which the genitals were not covered by underwear or by dusting the vulva with starch-containing powders; or (3) by perverse adult persons (very rarely).

The clinical manifestations are (1) a foul-smelling, purulent, profuse, often hemorrhagic discharge and (2) vaginal hemorrhage (without signs of precocious puberty). Auxiliary examinations include sounding of the vagina, bimanual rectal examination, x-ray examination of the pelvis, and vaginal endoscopy. After removal of the foreign body both discharge and hemorrhage subside very quickly.

FROM THE AUTHOR'S SUMMARY.

Chronic Infectious Diseases

TREATMENT WITH STREPTOMYCIN OF MILIARY TUBERCULOSIS AND TUBERCULOUS MENINGITIS. J. VALTIS, S. MANGRIOTI, and S. CARPETANAKI, Presse méd. **58**:140 (Feb. 11) 1950.

At the hospital-sanatorium "Sortiria," near Athens, the authors treated with streptomycin 69 patients proved to have miliary tuberculosis or tuberculous meningitis. Although the amounts used were limited by the scarcity of the drug, there was definite evidence of its usefulness, especially in miliary tuberculosis. There was a better response to treatment when tuberculous meningitis was not accompanied with generalized miliary tuberculosis.

DAFFINEE, Melrose, Mass.

VACCINATION WITH BCG. A. COURCOUX, Presse méd. **58**:200 (Feb. 25) 1950.

A law passed in France Jan. 5, 1950, makes it mandatory to vaccinate certain categories of the population with BCG. It is to be hoped that eventually this will be extended to include all tuberculin-negative persons.

Courcoux summarizes the important points in the use of BCG. Newborn infants may be vaccinated as soon as birth weight is attained and the infant is doing well. Older children first have a tuberculin test done. Scratches are made through three drops of vaccine 1 cm. apart, the scarification extending into the subcuticular area enough to draw blood. The vaccine is left in contact with the skin 15 minutes, and a dressing is applied. No contact with tuberculous persons should be allowed for two months. If the tuberculin reaction is still negative after three months, vaccination should be repeated.

DAFFINEE, Melrose, Mass.

TUBERCULOSIS IN AN INFANT WITH EXTENSIVE INVOLVEMENT OF ADRENAL GLANDS, TREATED WITH STREPTOMYCIN. G. DOLIVO, Helvet. paediat. acta **4**:542 (Dec.) 1949.

Primary tuberculosis focus with extensive miliary tuberculosis was found in the lung of an infant. The miliary spreading was cured with streptomycin, but in the region of the primary infiltrate, caseation took place and a cavity was formed. The autopsy showed extensive damage to both adrenal glands from large tuberculous nodules. Histologically these nodules were clearly seen to be partially healed.

FROM THE AUTHOR'S SUMMARY.

SIGNIFICANCE OF BRONCHIAL PERFORATION IN TUBERCULOSIS OF ENDOTHORACIC LYMPH NODES. O. GÖRGÈNYI-GÖTTCHE and O. KASSAY, Schweiz. med. Wchnschr. **80**:1213 (Nov. 11) 1950.

The authors want to state that they fully realized the significance of bronchial perforation of tuberculous lymph nodes, contrary to the claim of P. Schwartz. Such a perforation was found in 47.1% of children examined, who had died of tuberculosis. The postmortem examination is to be performed with special care. The bronchoscopic examination demonstrated the perforation in a little more than one-half of the cases. Such a perforation occurs frequently and may be relatively benign.

AMBERG, Rochester, Minn.

ALLERGOMETRY, BLOOD SEDIMENTATION RATE, AND ARNETH'S INDEX IN THE COURSE OF CHILDHOOD TUBERCULOSIS UNDER STREPTOMYCIN THERAPY. G. FIORAVANTI, Lattante **21**:573 (Sept.) 1950.

In 30 children with tuberculosis, the allergy to tuberculin usually increased, the blood sedimentation rate decreased, and Arneth's index remained unchanged while streptomycin therapy was yielding beneficial results.

HIGGINS, Boston.

MENINGITIS FROM MYCOTORULA ALBICANS IN AN INFANT WITH ACUTE MILIARY TUBERCULOSIS. E. REZZA, Minerva pediat. **2**:587 (Dec.) 1950.

An undernourished child of 19 months had anorexia, cough, vomiting, and intermittent fever; the tuberculin reaction was positive, and a chest roentgenogram revealed miliary lesions, diagnosed as miliary tuberculosis. Lumbar puncture yielded normal fluid. Treatment with streptomycin was given; streptomycin was also given intrathecally each week as a prophylactic measure against possible meningitis. After three months meningeal signs appeared; the spinal fluid gave a cell count of 260 cells and a positive Pandy reaction. Cultures of the spinal fluid after two weeks were reported positive for blastomycetes. The diagnosis of tuberculous meningitis was then changed, and treatment with iodides was begun. The symptoms slowly cleared up; the spinal fluid was normal after 10 weeks. The chest roentgenogram showed clearing of the miliary pathologic changes. The child began to gain weight and was reported to be in excellent health four months later.

HIGGINS, Boston.

GLUTATHIONE IN SPINAL FLUID OF PATIENTS WITH TUBERCULOUS MENINGITIS AND UNDER TREATMENT WITH STREPTOMYCIN. F. MULÉ and L. GARUFI, Pediatria **58**:325 (May) 1950.

Analyses were made to determine the glutathione content of 64 spinal fluids from 15 patients with tuberculous meningitis who were under treatment with streptomycin. The glutathione content was found to increase when the child was showing clinical improvement and to fall as the child's condition became worse.

HIGGINS, Boston.

MENINGOENCEPHALITIS FROM TOXOPLASMA. F. MULÉ, Pediatria **58**:381 (May) 1950.

Convulsions developed in a 13-day-old infant. On lumbar puncture, a clear fluid, not under pressure, was obtained. The Pandy reaction was positive; the spinal fluid sugar content was normal; a slight sediment, on centrifuging the fluid, was found to contain some lymphocytes and polymorphonuclear leucocytes and some elements which appeared to be Toxoplasma. The child showed some improvement under treatment with calcium bromide, sulfonamides, and penicillin but shortly afterward had a relapse and died. At autopsy a gelatinous exudate was observed over the brain. The parasite was cultured on chick embryo tissue.

HIGGINS, Boston.

STREPTOMYCIN IN THE TREATMENT OF THE TROUBLESOME ALLERGIC-EXUDATIVE PHASE OF PRIMARY TUBERCULOSIS. M. RAMAGLIA and E. MIRAGLIA, Pediatria **59**:200 (March) 1951.

On the basis of 22 cases of primary tuberculosis in the allergic-exudative phase in children, treatment with streptomycin was found not to be beneficial. It would appear that streptomycin may disturb the immunizing activity of the body against the tubercle bacilli. When the tubercle bacilli have become localized, streptomycin therapy is beneficial.

HIGGINS, Boston.

CHOLINESTERASE IN THE CEREBROSPINAL FLUID OF CHILDREN WITH TUBERCULOUS MENINGITIS. S. CUTILLO and C. BRANDI, Pediatria **59**:229 (March) 1951.

Using Ammon's method, the authors determined the cholinesterase content of the spinal fluid of 34 of 38 patients with tuberculous meningitis and found it to be higher than in normal spinal fluid. In the later stages of the streptomycin therapy of the disease, this enzyme action had become more nonspecific, in that it was not inhibited by caffeine and sodium benzoate.

HIGGINS, Boston.

CONGENITAL SYPHILIS OF THE LUNGS IN A GIRL OF 17 MONTHS. G. CROCCO, Pediatria **59**:247 (March) 1951.

A case report including autopsy data is accompanied with a lengthy clinical and histopathological discussion of pulmonary syphilis.

HIGGINS, Boston.

RESISTANCE OF KOCH BACILLUS TO ANTIBIOTIC DRUGS. PIERO MOGGI, Riv. clin. Pediat. **48**:161 (March) 1951.

The author, after having presented the theories of bacterial resistance to antibiotics and its biological characteristics, analyzes the clinical and experimental results of the resistance of Mycobacterium tuberculosis to streptomycin, sulfonamides, paraaminosalicylic acid, tibione, and neomycin and suggests a better therapeutic use of antibiotics to prevent streptomycin resistance.

FROM THE AUTHOR'S SUMMARY.

CLINICAL ASPECTS OF TUBERCULOUS MENINGITIS IN CHILDREN WHO RECEIVED PROTRACTED STREPTOMYCIN THERAPY. R. GARSCHE and F. SOUCHON, Arch. Kinderh. **138**:113 (Feb.) 1950.

Of a total of 25 children with tuberculous meningitis who were treated with streptomycin, 7 died. The authors try to establish two distinct types of tuberculous meningitis. In the first type the meningitic syndrome and the encephalotoxicosis disappear under streptomycin therapy within less than three months. Clinical observation during the following six to nine months reveals no pathologic change, and the spinal fluid remains normal. In the second type the clinical symptoms improve under streptomycin therapy in the beginning, but early symptoms of cerebral damage become manifest which are designated by the authors as "encephalopathy." It is unpredictable which course the disease will take. Therefore, streptomycin therapy should always be continued for longer than six weeks. Attention should be paid to the prevention of hydrocephalus.

ARON, Chicago.

BLOOD TRANSFUSION IN CHILDREN WITH ADDITION OF OXIDE OF ARSENIC AS PROTECTION AGAINST TRANSFUSION SYPHILIS. JOACHIM BROCK and GERHARD CONRADI, Deutsche med. Wchnschr. **75**:1021 (Aug. 11) 1950.

To exclude risk of transfusion syphilis, it is recommended that to fresh citrated blood, which is preferred for transfusion, be added one of the arsenic preparations prepared by Hoechst Dye Works (#11563 A and 11801 B). Such transfusions were given to 661 infants and 278 children. With the amounts given, no side-effects were noted.

AMBERG, Rochester, Minn.

SEROLOGICAL STUDY MADE IN CHILDREN TREATED WITH STREPTOMYCIN. O. TEYSCHL, Pediat. listy **5**:196 (No. 4) 1950.

The cerebrospinal fluid of patients suffering from tuberculous meningitis does not acquire any antigenic qualities which could be utilized for the serological diagnosis of tuberculosis, although a great number of Mycobacterium tuberculosus (Koch bacilli) are being destroyed throughout the protracted period of treatment. There is a much smaller amount of complement in the cerebrospinal fluid of these patients than in their blood serum. This fact proves that the disturbance of the blood-cerebrospinal barrier is not significant. In the serum of streptomycin-treated patients no antibodies could be detected. This indicates that the patients do not become streptomycin-resistant even during protracted treatment.

FROM THE AUTHOR'S SUMMARY.

NEUROLOGICAL FINDINGS IN TUBERCULOUS MENINGITIS. K. BRACHFELD and J. SVATY, Pediat. listy **5**:215 (No. 4) 1950.

The authors discuss the neurological symptomatology of 185 cases of tuberculous meningitis in which streptomycin was used. The cases are divided into four groups. The first group is comprised of the patients with pure meningeal signs without any focal signs. The second group,

of 53 cases, consists of patients who exhibited focal signs which either have already subsided or still exist to varying degrees. The third group includes 57 children who had neurological signs lasting longer than six weeks. The authors consider these cases to have been influenced by the streptomycin therapy. The gravest problem in this group is chronic hydrocephalus. Finally, the fourth group is formed by the 46 cases in which death ensued within six weeks. In these cases streptomycin therapy did not significantly influence either the course or the symptomatology of the illness. The significance of neurological examination as an aid to making a prognosis and in indicating the necessity for surgical intervention is discussed.

FROM THE AUTHORS' SUMMARY.

SOME EXPERIMENTS CONCERNING ANTITUBERCULOUS IMMUNITY PRODUCED WITH THE AID OF RADIOACTIVE BACILLI. L. STROM and G. WIDSTROM, Acta Pædiat. **40**:213 (May) 1951.

Studies of the passage of radioactive tubercle bacilli through guinea pigs and of the dissemination of these bacilli in the various organs, as well as of their concentration in the urine and the blood, are reported. Elimination of the marked substance is found to be increased in the immunized animals, which might be interpreted as an indication of immunity and might further indicate the degree of that immunity.

FROM THE AUTHORS' SUMMARY.

OCCLUSION OF ARTERIA DORSALIS PEDIS IN A CHILD WITH MILIARY TUBERCULOSIS. HANS TALLQVIST, Nord. med. **39**:1464 (Aug. 6) 1948.

The author cites three previously published cases and reports a case of his own in which arterial occlusion, due to arteritis, was found in a child suffering from generalized tuberculosis.

WALLGREN, Stockholm, Sweden.

STREPTOMYCIN THERAPY IN TUBERCULOSIS MENINGITIS. S. VAN CREVELD and M. R. H. STOPPELMAN, Maandschr. kindergeneesk. **17**:77, 1949.

The authors' experiences with administration of streptomycin to seven children with tuberculous meningitis are given. The ages of the patients varied between 15 months and 6 years. Five patients were admitted in a late phase of the disease. Three children recovered, two of whom show severe mental and neurological changes. The other one is still in excellent condition one and one-half years after therapy was started. Three patients had tuberculous meningitis and miliary tuberculosis of the lungs.

In all cases tubercle bacilli were isolated from the spinal fluid. In one case no changes in the lungs were found at autopsy; one mesenteric node was enlarged. From this lymph node as well as from the spinal fluid tubercle bacilli of the bovine type were cultured. In the other cases the tubercle bacilli were of the human type.

In five children 45 mg. of streptomycin per kilogram of body weight daily were injected intramuscularly and 25 to 100 mg. daily intrathecally. One child was treated with streptomycin and glucosulfone sodium (promin®); 25 mg. of streptomycin per kilogram of body weight daily were given intramuscularly and 15 mg. intrathecally. Twice a day 400 mg. of glucosulfone sodium was injected intravenously. The seventh patient, who recovered without defects, received 45 mg. streptomycin during the first 10 days and then 90 mg. of streptomycin per kilogram of body weight daily during a period of five months. In some cases paraaminosalicylic acid was also administered.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Blood, Heart and Blood Vessels and Spleen

ELECTROCARDIOGRAPHIC CHANGES OCCURRING DURING THE COURSE OF REPLACEMENT TRANSFUSIONS. ROBERT A. FURMAN, HERMAN K. HELLERSTEIN and VIOLA STARTZMAN, J. Pediat. **38**:45 (Jan.) 1951.

Serial electrocardiograms were taken during the course of replacement transfusion with citrated blood. Changes typical of hypocalcemia were observed, although these changes were not demonstrable in total serum calcium measurements. One gram of calcium given intra-

venously at the conclusion of the transfusion corrected the electrocardiographic changes. This amount of calcium is adequate for a 500-cc. transfusion, regardless of the size of the baby. But at least five minutes should be allowed for administration of the calcium, 10 cc. of 10% calcium gluconate, to avoid signs of hypercalcemia.

MACDONALD, Pittsburgh.

THYMECTOMY AND ACTH IN LYMPHATIC LEUCEMIA. A. M. EARLE, W. A. REILLY and G. O. DEAN, J. Pediat. **38**:63 (Jan.) 1951.

Four patients with lymphatic leukemia had temporary remissions of the disease after thymectomy. Further improvement followed corticotropin (ACTH) therapy which was started during the remissions. However, all four patients had relapse. The combined procedures do not seriously affect the ultimate course of leukemia.

MACDONALD, Pittsburgh.

ROENTGEN FINDINGS IN SICKLE-CELL ANEMIA. DAVID S. CARROLL and J. W. EVANS, Radiology **53**:834 (Dec.) 1949.

The symptomatology is so varied and complex for sickle cell anemia that it may masquerade as many different diseases. The roentgenologic findings in sickle cell anemia have been outlined as follows:

A. Long bones
   1. Thinning of cortex and widening of medullary cavity
   2. Prominent trabeculation
   3. Thickening of the cortex with narrowing of the medullary cavity
   4. Periosteal elevation
   5. Bizarre bone architecture with replacement fibrosis

B. Skull
   1. Osteoporosis and widening of the diploe
   2. Thickened skull, usually in localized areas
   3. Perpendicular striation

C. Pelvis and spine
   1. Osteoporosis with accentuated trabeculation
   2. Biconcave vertebrae

D. Chest
   1. Enlarged heart
   2. Osteoporosis and accentuated trabeculae of the ribs
   3. Pulmonary edema
   4. Pulmonary thromboses

A definite diagnosis of sickle cell anemia can be made from roentgenograms in only a few cases.

ANSPACH, Chicago.

THREE CASES OF THALASSAEMIA OCCURRING IN ONE FAMILY. TAHIA FAHMY and MOUSTAFA KINAWY, J. Roy. Egyptian M. A. **34**:133, 1951.

The authors present case reports of three siblings with familial erythroblastic anemia (Cooley's anemia or thalassemia).

MCGUIGAN, Evanston, Ill.

DIAGNOSIS OF OPEN BOTALLI'S DUCT. A. BUHLMANN and C. MAIER, Schweiz. med. Wchnschr. **80**:1185 (Nov. 4) 1950.

Bayer and Landen have stressed the value of the reduction of a respiratory minute volume on breathing of a high-percentage oxygen mixture, believing that when it is used in conjunction with other tests, angiocardiography can be dispensed with. Buhlmann and Maier state that when the diagnosis of patent ductus arteriosus by the usual clinical methods is not certain, only catheterization of the heart with angiocardiography, gas analysis, and intracardial pressure determination can confirm the diagnosis before surgical intervention.

AMBERG, Rochester, Minn.

DIAGNOSIS OF OPEN BOTALLI'S DUCT. O. BAYER and H. C. LANDEN, Schweiz. med. Wchnschr. **80**:1186 (Nov. 4) 1950.

The authors answer the criticism advanced against the value they placed on the decrease of the respiratory minute volume on breathing of oxygen-rich mixtures for the diagnosis of patent ductus arteriosus.

AMBERG, Rochester, Minn.

ABSORPTION BY THE INTESTINES OF HEMOLYSINS IN THE NEWBORN GUINEA PIG. G. BROGI and R. BIAGINI, Clin. Pediat. **32**:585 (Nov.) 1950.

When a serum containing hemolysins was fed orally to guinea pigs a few days old, an anemia developed in the animals. If the serum was fed together with bile in order to facilitate absorption, an acute and fatal anemia developed in the guinea pigs. After the guinea pigs were 20 days old, similar tests did not produce anemia, even when much larger amounts of the serum were given.

HIGGINS, Boston.

APPEARANCE OF BONE MARROW AND BLOOD SMEARS OF CHILDREN IN INSTITUTIONS. E. COSSANDI and M. CLERICI, Clin. Pediat. **33**:165 (March) 1951.

Ten pairs of children were used in this study. One child of each pair lived in an orphanage, and the other lived at home. The two children in each pair were of the same age and weight. The children were between 2½ and 4½ years old. In eight of the 10 pairs the children in the orphanage had a definitely higher percentage of lymphocytic cells in the smears.

HIGGINS, Boston.

ACUTE LEUKEMIA IN CHILDREN. E. CIFARELLI, Minerva Pediat. **2**:248 (June) 1950.

Cifarelli comments that the literature on the cytology of acute leukemias appears confusing and discordant at present, the distinction of the different hematological types being frequently based on the personal opinion of the single research worker.

HIGGINS, Boston.

CLINICAL VARIETIES OF ACUTE LEUKEMIA IN CHILDREN. A. SCHIAVINI, Minerva Pediat. **2**:255 (June) 1950.

Data on acute leukemia are assembled from the literature, and a few new cases are added, with comments about age and sex ratios, duration of illness, symptoms, and cytology.

HIGGINS, Boston.

CHEMICAL CRITERIA IN CYTOLOGICAL DIAGNOSIS OF ACUTE LEUKEMIA. E. STORTI and S. PERUGINI, Minerva Pediat. **2**:272 (June) 1950.

In differentiating cells in smears of leukemic blood, the Sudan-black-B-Giemsa or the May-Grünwald-Giesma stains are preferable to those involving the peroxidase reaction. The blood cells of acute leukemia are not necessarily very immature cells, but promyelocytes or myelocytes may predominate.

HIGGINS, Boston.

"LEUKEMIA" IN PEDIATRIC HOSPITAL PRACTICE. A. TENCONI, Minerva Pediat. **2**:276 (June) 1950.

Two cases of leukemia are reported; the establishment of the exact type presented difficulty.

HIGGINS, Boston.

CASE OF CHRONIC MYELOID LEUKEMIA TREATED WITH URETHAN. P. MARUSSI-SCARIZZA, Minerva Pediat. **2**:278 (June) 1950.

A child with chronic myeloid leukemia was followed over a period of five years. At first roentgen treatments were beneficial, but later they were ineffective. Urethan was then used, being given either orally, intramuscularly, or by clysis. The urethan led to a diminution in

the size of the spleen and a definite fall in the white blood cell count, in one instance to as low as 3,200; occasionally the urethan administration was followed by an immediate paradoxical rise in the white blood cell count, which, however, was followed by a fall. Just before the patient died, the leukemia entered an acute phase; this phase was not benefited by urethan medication.

HIGGINS, Boston.

LEUKEMOID REACTION IN AN INFANT. E. COSSANDI, Minerva Pediat. **2**:284 (June) 1950.

A 9-month-old infant during the course of a staphylococcic empyema began to show myeloblasts, promyelocytes, and myelocytes in the peripheral blood and more immature cells in the bone marrow than are usually found.

HIGGINS, Boston.

REMISSION IN CASE OF ACUTE LEUKEMIA. M. L. LONATI, Minerva Pediat. **2**:284 (June) 1950.

A 2½-year-old infant with acute leukemia had a remission lasting one month after treatment with an antibiotic ("sintomycetin").

HIGGINS, Boston.

"RHEUMATOID TYPE" OF ACUTE LEUKEMIA IN CHILDREN. M. NEGRI, Minerva Pediat. **2**:285 (June) 1950.

An early differential diagnosis of the rheumatic type of acute leukemia may be established by the finding of a rapid sedimentation rate, failure of response to salicylate therapy, granulocytemia, anemia, and the presence of abnormal cells in the peripheral blood. A bone marrow biopsy is indicated in suspected cases.

HIGGINS, Boston.

CASE OF VERY ACUTE LEUKEMIA WITH EARLY MASTOID LOCALIZATION. G. C. ABBA and C. GATTI-MANACCINI, Minerva Pediat. **2**:287 (June) 1950.

The presenting symptom in the case of a child with rapidly fatal acute leukemia was a very painful osteitis of the mastoid bone.

HIGGINS, Boston.

WOLFF-PARKINSON-WHITE SYNDROME WITH PAROXYSMAL TACHYCARDIA IN A FOUR-YEAR-OLD GIRL. R. BULGARELLI, Minerva Pediat. **3**:169 (March) 1951.

Attacks of paroxysmal tachycardia were first observed toward the end of the child's first year of life and had occurred at intervals of two to three months. A thorough cardiac study, including electrocardiograms and roentgenograms, was made during an attack lasting 24 hours and during various physiological tests (as forced breathing and oculocardiac reflex) and pharmacological tests (as with atropine, ergotamine, epinephrine, acetylcholine, and quinidine). The belief is expressed that the presence of congenital accessory conducting bundles explain the etiology and the pathogenesis of the paroxysmal tachycardia.

HIGGINS, Boston.

CASE OF HEMOLYTIC ICTERUS. DIEGO M. GUIGON COSTA, Acta pediat. españ. **89**:577 (May) 1950.

Costa reports the case history of a 3½-year-old boy in whom icterus developed at the age of 18 months. The family history was negative except for tuberculosis in the maternal grandfather. The spleen and liver were enormously enlarged; the skin was a violent yellow, as were the sclerae, and the gums were spongy. The blood test showed a white cell count of 16,500, hemoglobin 30%; a red cell count showed numerous microcytes, deeply stained and without the central depression (microferrocytes). An indirect van den Bergh test showed 10 mg. per 100 cc. of bilirubin. The urine showed a 3+ reaction for urobilinogen, 4+ for urobilin, and no bilirubin; feces also showed a 3+ reaction for urobilinogen. The spleen on removal weighed 460 gm. The child improved rapidly, but although all other symptoms have disappeared, the leucocytosis and the microferrocytes still persist.

Although splenectomy does not always produce such a radical change, and there are writers who report recurrences following splenectomy, the author feels it was the only possible treatment in this case.

ALLEN, Santa Fe, N. M.

PERIARTERITIS NODOSA IN CHILDHOOD. HEINZ HUNGERLAND and URSULA GREIFELT, Arch. Kinderh. **139**:12, 1950.

The authors give a detailed description of the case of a 17-month-old boy for whom the diagnosis of periarteritis was made during life. A critical analysis of 34 childhood cases of periarteritis and a thorough discussion of etiological theories, various localizations, and differential diagnosis are given. The authors emphasize that the prognosis is not so hopeless as is generally assumed. Not one of the many theories of causation is satisfactory.

GOTTSTEIN, Chicago.

CAPILLAROSCOPIC INVESTIGATIONS IN CHILDHOOD AND THEIR CLINICAL SIGNIFICANCE. HERBERT GROSS, Wien. klin. Wchnschr. **63**:344 (May 11) 1951.

The capillaries of the nail fold were studied in cases of nephritis, nephrosis, diabetes, erythrodermias, and other disorders. Special attention is called to the changes of the capillaries in nutritional disorders of infants and to the changes seen in cases of pneumonia in infants. Observation on the action of drugs on the circulation are given. Such observations can be of value in determining the administration of the drugs. Finally, the changes in the capillaries in diphtheria are outlined.

AMBERG, Rochester, Minn.

NIEMANN-PICK DISEASE. V. ZORIN and M. MITERA, Pediat. listy **5**:172, 1950.

The authors give a detailed description and analysis of a case of Niemann-Pick disease. Complete diagnosis was made from examination of the fundi, sternal puncture, puncture of the spleen, and biopsy of a lymph node while the patient, a 14-month-old girl of non-Jewish origin, was living. A differential-diagnosis survey and analysis of clinical and laboratory findings concerning the child and her parents is added. Pathological indications were increased chlorides and diminished calcium in the serum, increased level of globulins and thereby decreased albumin-globulin ratio, slightly decreased hematocrit value, decreased level of neutral fats and lecithin, and increased sedimentation rate of the red blood cells. All investigations of the parents showed them to be normal.

FROM THE AUTHORS' SUMMARY.

ACUTE FORM OF GAUCHER'S DISEASE IN THREE SIBLINGS. L. STRENGERS, Maandschr. kindergeneesk. **17**:237, 1949.

In a family of seven siblings the three younger ones all died at the age of about 10 months from the acute form of Gaucher's disease. They showed splenohepatomegally, opisthotonos in such a degree that the children were unable to lie supine, strabismus, and a ghastly pale color. The Gaucher cells in the material from puncture of the tibia were not characteristic at the onset of the disease, but later they were typical. Splenectomy was performed on one of the children, but this operation did not prevent death of the child, which occurred half a year later. Roentgenograms of the lungs showed shadows issuing from the hilus in the form of a fan. At autopsy Gaucher cells were found in the lungs. Though during life distinct cerebral disturbances were present, at autopsy no deviations could be found in the cerebrum.

Neither the mother nor the other children showed any morbid symptoms, but examination of the bone marrow could not be performed. The father, who had no complaints, was found to be suffering from a myeloid leukemia.

VAN CREVELD, Amsterdam, Netherlands.

LEUKEMIA IN CHILDREN: SOME NEW ASPECTS OF DIAGNOSIS AND TREATMENT. S. VAN CREVELD, Nederl. tijdschr. geneesk. **93**:3938 (Nov. 19) 1949.

On the basis of some personal experiences, the author discusses the value of leukemic changes in the roentgenograms of the knees for establishing the diagnosis of leukemia, especially when the clinical picture resembles rheumatic fever.

Substitution transfusion was unsuccessful in three patients; 4-aminopteroylglutamic acid (aminopterin®), an antagonist of folic acid, was given to a 5-year-old boy and a 3-year-old girl. The enlarged glands, liver, or spleen, diminished in size, but the leucocyte, erythrocyte, and

thrombocyte counts also dropped considerably. At autopsy, however, no leukemic changes in the liver could be demonstrated in the boy. The girl was still living at the time of writing. Examination of her bone marrow did not show any changes resulting from 4-aminopteroylglutamic acid therapy. During this treatment bands of calcification were noted on the roentgenogram of the knees, resembling those of lead poisoning.

Nothing definitive can be said about the value of folic acid as a therapeutic agent in leukemia, principally owing to the well-known whimsical course of this disease.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

THE TONSIL PROBLEM IN CHILDREN. N. BAUERJEE, Indian J. Pediat. **17**:185 (Oct.) 1950.

The indications for tonsillectomy are briefly discussed. The author's feelings on the subject agree for the most part with current practice in this country. McGUIGAN, Evanston, Ill.

Diseases of Lungs, Pleura and Mediastinum

AN EVALUATION OF RADIUM TREATMENT TO THE NASOPHARYNX IN ASTHMATIC CHILDREN VICTOR L. COHEN and WILBUR J. FISHER, J. Allergy **20**:328 (Sept.) 1949.

The authors studied 15 patients ranging in age from 4 to 16 years. All had perennial asthma and had skin reactions positive to various antigens.

The nasopharynx was exposed to 100 mg. of radium for six and one-half minutes. Four treatments at intervals of 21 days were given.

The authors feel that radium treatment to the nasopharynx is not a panacea for any type of asthma, but that it should be considered as an auxiliary to other forms of treatment.

It would appear that better results might be anticipated in a case with an increased sedimentation rate, normal sinuses, and little or no adenoid tissue in the nasopharynx.

HOVER, Cincinnati.

PNEUMONIA IN CHILDREN FOLLOWING THE INGESTION OF PETROLEUM PRODUCTS. C. H HEACOCK, Radiology **53**:793 (Dec.) 1949.

In a 3½-year period 156 children were admitted to the John Gaston Hospital, Memphis, because of ingestion of petroleum products. Of these, 103 exhibited evidence of poisoning, and hospitalization was required for 1 to 15 days each. In 58 cases all the changes seemed to be limited to the lower lobes. Fever and cough were the only clinical signs in 32, but all showed roentgen changes in the cardiophrenic angles. In 17 of another group the clouded zones were large, patchy, and confluent but definitely not lobar. In nine cases the clouding was extensive and could be considered lobar. The roentgen changes were most pronounced in 24 to 36 hours after ingestion of the offending substance.

ANSPACH, Chicago.

THE PATHOGENESIS OF BRONCHIECTASIS. FELIX G. FLEISCHNER, Radiology **53**:818 (Dec.) 1949.

The author has furnished several graphic examples explaining the nature of bronchiectasis in various phases. Many cases considered bronchiectasis represented extensive areas of destruction as occur in abscesses and therefore were not truly bronchiectasis. The importance of atelectasis and the transient character of early bronchiectasis were recognized. In contrast to the normal bronchograms, there was nonfilling of the peripheral branches, which indicated either obstruction or impaired ventilation of the parenchyma surrounding the dilated bronchus, giving the picture of the "leafless tree" without exception. Organizing pneumonitis made permanent a mechanical disturbance similar to fibrosis, with shrinkage as in atelectasis, causing an early reversible atelectatic collapse to become a permanent crippling condition. Areas of consolidation or emphysema, if suitably distributed, cause an increased external dilating pull upon the bronchi.

ANSPACH, Chicago.

A Report on Two Cases of Mediastinal Tumors. Hassan Ibrahim, J. Roy. Egyptian M. A. **34**:139, 1951.

Two patients with mediastinal tumors were operated on. In both cases there was marked improvement, although the final outcome was hopeless.

McGuigan, Evanston, Ill.

Diseases of Gastrointestinal Tract, Liver and Peritoneum

Reliability of Roentgen Examination in Hypertrophic Pyloric Stenosis in Infants. Hans W. Hefke, Radiology **53**:789 (Dec.) 1949.

Of 210 patients for whom the roentgenologic diagnosis of pyloric stenosis was made, 205 were operated upon. The roentgenologic diagnosis was substantiated in all but two cases. Here portions of small bowel were incorrectly interpreted as the pyloric "string sign." This sign and the pyloric opening time are, according to the author, the most reliable means of diagnosing pyloric stenosis. The value of x-ray examinations exceeds that of the clinical examination, and they should be used oftener. The author does not believe that fluoroscopy is necessary for the diagnosis of pyloric stenosis.

Anspach, Chicago.

Neurogenic Appendicitis. J. G. Knoflach, Wien. klin. Wchnschr. **63**:37 (Sept. 1) 1950.

"Neurogenic" appendicitis can occur during childhood, although rarely. The clinical picture can hardly be differentiated from the usual one of appendicitis. The commonest sign is pain in the right lower quadrant, which was noted in 94% of 142 cases. A florid form is distinguished by the pathologist from an obliterating stage. In the florid form the neural tissue of the plexus mucosus proliferates, with formation of new blood vessels and eosinophilia, in the absence of parasites. The mucous membrane is still without lesion, and the production of mucus is increased. The number of the argyrophile cells is usually increased. The neural proliferation, characterized by a pronounced new formation of the terminal reticulum, penetrates the stroma and the submucosa. In the obliterating stage the mucous membrane is destroyed, and consequently the lumen is obliterated. This is often followed by neuroma-like hyperplasia of the terminal reticulum. In the muscularis propria a hyperplasia starting from the plexus myentericus can also be found, with pronounced proliferation of the terminal reticulum. This second stage was seen more frequently in the cases with operation. The neurogenic appendicitis is not inflammatory in character but a splintering of the normal appendical tissue by neural proliferations, which does not protect the organ from an inflammation. Since two-thirds of the patients who undergo surgery become symptom-free after operation, it is probable that in these patients the neurogenic changes were limited to the appendix.

Amberg, Rochester, Minn.

Congenital Idiopathic Dilatation of the Intestine (Megaintestine). M. Toman and E. Vanecek, Pediat. listy **5**:221 (No. 4) 1950.

A case of congenital idiopathic dilatation of the whole intestine (megaintestine) in a 10-week-old girl is reported. Achalasia might account for this anomaly. The histological changes of the celiac plexus support this idea. The clinical and pathological pictures are briefly discussed. There was no evidence of disease in the mother during the pregnancy.

From the Authors' Summary.

Thiocyanate Space of Body and Mineral Concentration of Erythrocytes in Severe Infantile Gastroenteritis. Niilo Hallman and Jyrki Kauhtio, Acta pædiat. **39**:347 (Nos. 4-5) 1950.

A study is made of the extracellular (thiocyanate) space and blood chemistry in 14 cases of severe infantile gastroenteritis. On admission, and in spite of evident dehydration, thiocyanate space was normal in eight patients, considerably higher than normal in three, and below normal in only three. During rehydration, thiocyanate space increased regularly and always unmistakably more than the corresponding gain in weight. While recovery was in progress, the values returned to normal.

At the beginning of treatment the potassium concentration of the erythrocytes was lowered in these patients and the sodium concentration increased. A certain correlation could be observed between these values and changes in thiocyanate space. It is suggested on the basis of this study that changes in cellular permeability probably occur in severe infantile gastroenteritis.

FROM THE AUTHORS' SUMMARY.

Nervous Diseases

THE NON-INFECTIOUS NATURE OF THE GUILLAIN-BARRÉ SYNDROME WITH A POSSIBLE EXPLANATION FOR THE ALBUMINO-CYTOLOGICAL DISSOCIATION. N. REITMAN and K. ROTHSCHILD, Ann. Int. Med. **32**:923 (May) 1950.

The Guillain-Barré syndrome is a clinical entity which is not often diagnosed, although its occurrence is not uncommon. The chief reason for this is the failure of all attempts to isolate an etiologic agent and the multiplicity of synonyms by which this form of neuritis is known.

Reitman and Rothschild report two cases fulfilling the criteria of the Guillain-Barré syndrome which are unusual in that they do not represent postinfectious phenomena. In one case the cause was bronchogenic carcinoma with metastases to the extradural fat, compressing the spinal cord and nerve roots from the seventh cervical to the eighth thoracic. The second case represents an unusual form of serum sickness following injection of tetanus antitoxin. This case showed most extensive neurologic involvement, with rapid and practically complete recovery.

The authors suggest a common anatomic basis for the Guillain-Barré syndrome, regardless of the etiologic agent. It is believed that the basic pathologic process consists in an obstruction to the perineural circulation of the cerebrospinal fluid as the nerve roots emerge from the cord, permitting absorption of fluid and electrolytes but preventing the absorption of the larger protein molecules. The characteristic albuminocytologic dissociation may be explained in this fashion.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.]

CARBONIC ANHYDRASE IN THE BRAIN OF THE NEWBORN IN RELATION TO FUNCTIONAL MATURITY. W. ASHBY and E. M. SCHUSTER, J. Biol. Chem. **184**:109, 1950.

From studies of the carbonic anhydrase content of the central nervous system of fetal cattle and of premature human infants, it was previously reported that this enzyme first appeared in greater amounts in the lower centers and that the maximum amount progresses to higher centers as the fetus develops. The enzyme was not found in the cerebrum of fetal cattle until the last month of gestation, during which it rapidly rose to an amount equal to half that of the adult animal. Although a similar progressive increase in the enzyme was shown in the human fetus, as studied in premature births, none was found in the cerebrum at eight months' gestation or in the cerebrum of an 8-lb. (3,600-gm.), full-term infant. Although this child was well developed, the cause of death was not evident. The normality of this finding for the central nervous system was therefore questioned. There is a late appearance of carbonic anhydrase in the cerebrum of the young of the dog, the cat, the rat, and the rabbit, animals born in an immature condition; this is in contrast to its presence at birth in the cerebrum of animals which are more mature when born, such as the calf and the guinea pig. The data suggest correlation between the appearance of the enzyme in the cerebrum and the beginning of cerebral functioning, as indicated by the parallel maturation of certain sense organs and the first appearance of alpha brain waves, as reported in the literature. The fact that there is an even later appearance of the enzyme in the central nervous system of the rat, dog, rabbit, and cat than in that of the human infant increases the probability that the absence, previously reported, of carbonic anhydrase in the cerebrum of the human newborn infant may be normal.

PAGE, Cleveland [A. M. A. ARCH. NEUROL. & PSYCHIAT.]

ASSOCIATION OF CONGENITAL SPASTIC QUADRIPLEGIA AND ANDROGENIC PRECOCITY IN FOUR PATIENTS. W. H. PERLOFF and J. H. NODINE, J. Clin. Endocrinol. **10**:721 (July) 1950.

Perloff and Nodine report on four children with congenital spastic quadriplegia associated with the premature development of pubic hair and elevated urinary 17-ketosteroid excretion.

The manifestations of androgenic stimulation are thought to be the result of precocious adrenarche, which occurs because of agenesis or destruction of a center in the brain located in or near the posterior hypothalamus, the function of which is to prevent pituitary stimulation of the androgenic zone of the adrenal until the time of puberty.

FRANKEL, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.]

TOTAL ABSENCE OF THE CEREBRAL HEMISPHERES. E. E. JOHNSON, MARY WARNER and J. P. SIMONDS, J. Pediat. **38**:69 (Jan.) 1951.

The authors describe two infants with total absence of the cerebral hemispheres associated with arhinencephalia. In both infants the adrenals were abnormally small owing largely to the absence of the androgenic zone.

MACDONALD, Pittsburgh.

MEDICAL ASPECTS OF CEREBRAL PALSY. MEYER A. PERLSTEIN, Nerv. Child **8**:128, 1949.

The author of this article is a well-known authority on the subject of cerebral palsy. This article is characteristic of the author's lucid, thorough, and excellently readable presentations. As one of the etiological factors of this condition the author includes a very excellent description of the Rh factor.

Those particularly interested in this subject will welcome the bibliography. It includes almost all that has been written on the subject in the English language since 1940.

WEINFELD, Highland Park, Ill.

BRAIN TUMORS IN INFANCY AND CHILDHOOD. SIDNEY W. GROSS, New York J. Med. **50**:2267 (Oct. 1) 1950.

Working in the departments of neurosurgery in Montefiore and Mount Sinai hospitals, New York, Gross made this report before the Medical Society of the State of New York at its annual meeting in May, 1950. Olfactory or visual hallucinations may be the first sign of brain tumor in the very young. Vomiting and enlargement of the head in infants make the diagnosis relatively easy. In older children headaches, failing vision, imbalance, and poor use of arms and hands should cause one to suspect cerebral lesion. One unusual instance is cited. A 2-month-old infant had the above symptoms for two days. Necropsy six weeks later disclosed "a large pineal tumor." Ventriculography "remains the most important diagnostic procedure in infancy and childhood." As to incidence, Gross states, "About 80 per cent of all tumors of the brain in individuals under fifteen years are gliomas." Craniopharyngiomas comprise an important group in early life. They are congenital and arise from cell rests in the craniopharyngeal duct. Operative mortality is still high in the very young, but "older children do surprisingly well." Careful preoperative localization and better surgical technique have reduced postoperative mortality greatly. Abandonment of the two-stage operation has helped, and, as a result, in most clinics at present surgical mortality does not exceed 10%.

VOORHEES, New York [A. M. A. ARCH. OTOLARYNG.]

INTRASPINAL AND INTRATHORACIC TUMOR WITH PARAPLEGIA IN A CHILD: REPORT OF A CASE. H. J. SVIEN, Proc. Staff Meet., Mayo Clin. **25**:715 (Dec. 20) 1950.

The incidence of tumors of the spinal cord in children is not very great. At the Mayo Clinic during a 10-year period only 37 cases were uncovered. The majority of the tumors were gliomas, neurofibromas, sarcomas, and lipomas. No ganglioneuromas were found. The hourglass type of tumor makes up only a small fraction of all tumors of the spinal cord (5 of the 37 cases of the present series).

A large variety of tumors occur in the mediastinum. The commonest tumor in the posterior mediastinum is of nerve origin. The hourglass, or dumbbell, tumors of the mediastinum are almost always of nerve origin.

Svien describes a 5½-year-old child who, after developing normally to the age of 1½ years, had progressive difficulty in walking until there were total paralysis of the lower extremities and incontinence of the bladder and bowel. Examination showed absence of abdominal reflexes and

the Babinski sign and ankle clonus bilaterally. Roentgenograms revealed a paravertebral mass from the 7th to the 11th thoracic vertebra. A diagnosis of intraspinal and intrathoracic tumor was made.

A bilateral thoracic laminectomy from the 7th through the 12th vertebra was done. This exposed a large encapsulated extradural tumor lying in the full extent of the laminectomy area. It could be seen that the tumor entered the spinal canal from the chest through the enlarged foramen between the 9th and 10th thoracic vertebrae. The intraspinal portion of the tumor was removed. Microscopic examination revealed a ganglioneuroma, relatively benign. The patient moved her legs on the fifth postoperative day and was able to void normally when the urethral catheter was removed on the eighth day.

Two weeks after the first operation the intrathoracic mass was removed. The main body of the tumor involved the sympathetic chain, the splanchnic nerves, and the three or four intercostal nerves which lay deep or external to it.

The patient's convalescence was uncomplicated, and when discharged 29 days after the operation on the spinal cord, she was able to walk without assistance. When she was reexamined four months later, there was no suggestion of recurrence. The only finding of note was some degree of scoliosis. Because of the favorable histologic diagnosis and the patient's satisfactory progress, the outlook was considered hopeful.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.]

RADIOLOGY IN NEUROSURGICAL CONDITIONS IN CHILDHOOD. NICHOLAS GOTTEN and C. D. HAWKES, Radiology **53**:798 (Dec.) 1949.

Neurosurgical conditions in which positive roentgenographic evidence was found are summarized, and special roentgenographic procedures are discussed. Cases illustrated include cranium bifidum with encephalocele, false porencephaly, hydrocephalus, colloid cyst of the third ventricle, teratoma of the pineal gland, medulloblastoma of the cerebellar vermis, metastatic neuroblastoma, cortical hemangioma, and cerebral arteriovenous anastomosis. The author believes that air injection in some cases may be correctly supplemented by arteriography.

ANSPACH, Chicago.

ARTERIOGRAPHY AND CAROTID ARTERY LIGATION IN INTRACRANIAL ANEURYSM AND VASCULAR MALFORMATION. I. S. WECHSLER, S. W. GROSS, and I. COHEN, J. Neurol., Neurosurg & Psychiat. **14**:25 (Feb.) 1951.

The authors report the results of ligation of the common carotid artery in the neck in 30 cases, including 17 cases of aneurysms of the circle of Willis, 9 cases of vascular malformations of the hemisphere, and 4 cases of carotid artery-cavernous sinus fistulas.

In the group with malformations no death occurred; in one case hemiparesis developed. In no case did bleeding recur after operation. Two patients continued to have convulsions. In the group with aneurysms there was one death nine hours after ligation. The other deaths in this group followed craniotomy, one after 10 days and one after 4 weeks. There was no recurrence of bleeding. There was one postligation hemiplegia with aphasia.

The authors feel that the mortality, morbidity, and results of this method of treatment compare favorably with those of other methods advocated for these conditions.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.]

BRAINS FROM STREPTOMYCIN-TREATED CASES OF TUBERCULOUS MENINGITIS. G. PAYLING WRIGHT and R. J. W. REES, Proc. Roy. Soc. Med. **41**:456 (July) 1948.

Examinations of the brains and spinal cords from three children, aged 30 to 34 months, who died of tuberculous meningitis revealed similar pictures. Each patient had received eight to nine weeks of treatment with streptomycin intramuscularly and intrathecally before death and had shown a progressive decrease in the number of cells in the cerebrospinal fluid. Primary lesions were found in the lungs in each case. There was a thick, yellowish, gelatinous exudate, most pronounced in the interpeduncular fossa, containing large numbers of tubercle bacilli. These

organisms were found to be sensitive to streptomycin. Each brain showed a considerable degree of symmetrical hydrocephalus.

BERRY, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.]

HEREDITY IN HEPATOLENTICULAR DEGENERATION AND INTRINSIC RELATION OF WESTPHAL-STRÜMPELL PSEUDOSCLEROSIS AND WILSON'S DISEASE: NOSOLOGICAL PLACE OF KEHRER'S "ABDOMINAL WILSON'S DISEASE" IN HEPATOLENTICULAR DEGENERATIONS. MICHEL J. ANDRÉ and LUDO VAN BOGAERT, Encéphale **38**:1, 1950.

André and van Bogaert indicate that Wilson did not consider the disease named after him as congenital or abiotrophic, but he did believe that it could be familial. Even as late as 1947, in his "Neurology," he appeared to hesitate in believing that it was hereditary. In 1930, Kehrer arrived at the conclusion that hepatolenticular degeneration was a heredofamilial disease following a simple recessive mode of transmission. He was convinced that the neural lesions were secondary to those of the liver and that it was primarily on the liver that the hereditary factors bore most heavily. In 1939, Stadler added an important genetic study to the heredity of Wilson's disease. He insisted on the frequent presence of consanguinity of the ancestors of strains with the disease and the symptomatic homotypy of the cases in the same family. He agreed with Kehrer in considering the disease to be due to a simple recessive trait involving the polyglandular metabolism of the liver, the gastrointestinal tract, and, above all, the carbohydrate metabolism of the body.

The article reviews families showing hepatolenticular degeneration reported in the literature, with the pathologic changes noted in these families. In the fourth part of the paper the authors give full details and genealogic tables for five families with Wilson's disease already studied and previously reported by them, to which they now proceed to add the data of two more family strains never before published. They believe in the nosological unity of the various forms of Wilson's disease, such as pseudosclerosis, the abdominal form of the disease, and hepatolenticular degeneration, as well as certain obscure maladies of the liver and gastrointestinal tract coupled with neurologic or mental symptoms, which they consider to be part of this group.

The authors offer the following conclusions: Hepatolenticular disease is familial in 55% of the known strains and appears sporadically in 45%. They agree that it is due to a simple recessive gene. It can sometimes be transmitted directly, without, however, implying any dominance. According to Lisi, in the Insabato family there was direct transmission of Wilson's disease over four generations.

Genetic studies appear to indicate that the majority of pathologic disturbances noted either in the ancestry or the collaterals were psychiatric (from simple psychasthenia to dementia), neurologic (usually extrapyramidal), or gastrointestinal (stomach, liver, biliary tract). The frequency of gastric carcinoma in certain strains merits attention. The authors' studies of families bear out the conclusions of Kehrer. They affirm the neuropathologic unity of hepatolenticular degeneration in the light of their own data. However, they are not prepared to decide as to the fundamental unity of the various forms. They note that hepatic cirrhosis, at least in any clinical form, is known in the neurologically normal progenitors of any of the subjects with hepatolenticular degeneration. In tainted families Wilsonian cirrhosis without neurologic signs is unusual (less than 10% of cases of hepatolenticular degeneration).

Genetic studies have not proved that pseudosclerosis and pure Wilson's disease coexist in the same family. The abdominal form of Wilson's disease lies on the border between the classic type of hepatolenticular degeneration and pure Wilsonian cirrhosis without specifically detectable neurologic signs. The study of this abdominal type will resolve the problem of the real unity of the hepatolenticular-degenerative group of diseases.

ZINKIN, New York [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

CONTRIBUTION TO THE TREATMENT OF SPASTIC PARALYSIS: CURARIZING AGENT AS AN AID TO PHYSIOTHERAPY. J. MICHAIL, Presse méd. **58**:4 (Jan. 7) 1950.

The author reports encouraging results in the treatment of spastic paralysis. Seventeen children (11 of them having cerebral spastic infantile paralysis, or Little's disease) were given

intramuscular injections of chondodendron tomentosum extract, purified (intocostrin®), three-fourths of a unit per kilogram of body weight. Two children showed little or no response, but the others showed a remarkable relaxation within an hour. This relaxation often lasted several days.

By this method of relaxing the musculature, the use of physical therapy becomes practicable without the necessity for surgical operation. Massage and manipulation can be performed with a minimum of suffering for the patient.

DAFFINEE, Melrose, Mass.

ARNOLD-CHIARI MALFORMATION. A. RICHARD and P. F. GIRARD, Rev. neurol. **81**:332 (May) 1949.

The Arnold-Chiari malformation consists of displacement of the medulla and lower portion of the fourth ventricle and cerebellum into the cervical canal. This is accompanied with distortion of the medulla, lengthening of the lower cranial nerves, and protrusion of a tongue of cerebellum through the foramen magnum into the cervical canal. The flow of cerebrospinal fluid is blocked, and hydrocephalus accompanies the condition frequently. Other malformations, such as spina bifida, platybasia, and assimilation of the atlas, may, and often do, exist. Complications, such as syringobulbia, cerebellar degeneration, and adhesive arachnoiditis, may also exist. The frequent association of spina bifida with the deformity has led to the theory that the downward traction on the contents of the posterior fossa is due to fixation at the site of the dysraphia.

The authors report the case of an 11-year-old girl who was admitted for headache, vertigo, stiff neck, papilledema (5D.), paralysis of the left sixth cranial nerve, labyrinthine difficulties, and cerebellar difficulties, particularly in walking. There were no pyramidal signs. Operation and removal of the posterior border of the foramen magnum and opening of the fourth ventricle relieved the intracranial hypertension.

The authors note the following symptoms and signs of the syndrome: (1) intracranial hypertension; (2) signs referable to the lower cranial nerves; (3) signs of compression of the brain stem, most frequently nausea, vomiting, and vascular signs, with signs of involvement of the long tracts not frequent, and (4) cerebellar signs.

Roentgenograms reveal only signs of increased intracranial pressure or another accompanying deformity, such as platybasia, which, in turn, may lead to the suspicion of accompanying Arnold-Chiari malformation. Spinal puncture usually reveals block, and injection of iodized oil U. S. P. reveals space-occupying cerebellar tissue high in the cervical canal.

The treatment is surgical and is aimed at relieving the traction and blockage, not at restoring the dislocated tissue to its normal site.

LEGAULT, Washington, D. C. [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

CASES OF PORENCEPHALY AND OF PARTIAL DILATION OF THE LATERAL VENTRICLES. R. RUGGERI, Pediatria **59**:104 (Jan.) 1951.

Two case reports are given. The first case was of a mentally deficient child who died during a grand mal attack; at autopsy porencephalic cavities were found in the cerebrum and in the cerebellum. The other case was of a child subject to epileptic attacks, mentally deficient, and with optic atrophy, total on the right and partial on the left. An air encephalogram revealed a marked dilatation of the occipital horn of both lateral ventricles. Cystic changes in the brain are caused by ependymitis, adhesions, and increased spinal fluid pressure. The primary cause of the condition in these cases is not clear.

HIGGINS, Boston.

MYOCLONIA HEREDITARIA MUSCULI MENTALIS. A. YDE, Acta psychiat. et neurol. **25**:111, 1950.

Yde describes a hereditary form of myoclonia musculi mentalis which occurs both in males and in females and can be transmitted through persons of either sex. There were seven known cases of the disease in the family studied.

The symptom presented consisted of fine, but rapid, myoclonic twitchings in the region of the chin, which persisted for a few moments to half a day. Other groups of facial muscles

were not involved; the myoclonic movements of the musculus mentalis did not affect the lower lip, and there were no accompanying sensory phenomena. The syndrome occurred as early as the second or third week of life and appeared independently of weeping or laughing.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

Psychology and Psychiatry

THE RELATIONSHIP BETWEEN INFANT FEEDING EXPERIENCE AND LATER BEHAVIOR. NILES RUMELY NEWTON, J. Pediat. **38**:28 (Jan.) 1951.

Newton has made an intensive study of the relationship between the behavior of a group of 5- to 6-year-olds and their early feeding experiences. It is accepted that the behavior of children is affected by early feeding experiences but that other factors, such as heredity, the father's attitude, and home environment, are also important. This study indicates that the cause and effect relationship between early feeding and later behavior is not very strong. More important, perhaps, is the attitude of the mother. It is the attitude of the mother that determines the type of feeding the infant receives and strongly affects his environment.

MACDONALD, Pittsburgh.

PROGNOSIS AS TO MENTAL DEVELOPMENT OF CHILDREN BORN BY CAESARIAN SECTION. M. SCHACHTER, Pediatria **59**:1 (Jan.) 1951.

Of 5,000 children examined for mental retardation or for neurological disturbances, only six had been born by Caesarian section. Five were mentally retarded, and one was an epileptic. In only two of these six did damage at birth appear to be the underlying cause of the deficiency.

HIGGINS, Boston.

PHENYLPYRUVIC OLIGOPHRENIA. OTTO LOAS MOHR, Tidsskr. norske lægefor. **68**:197 (May 1) 1948.

Of 2,400 feebleminded persons examined in Norway, 34 (19 females and 15 males) were found to have phenylpyruvic oligophrenia. The ages varied from 1½ to 63 years. The 34 cases are distributed among 22 groups of siblings; there were two persons affected in 12 of these groups and only one in 10 groups. These 22 groups of siblings consisted of 126 persons; thus, 27% of the total 126 suffered from phenylpyruvic oligophrenia. In addition, feeblemindedness had occurred in six other children, but these had died before the examination. In a case reported by Ruud the hereditary study revealed three new cases in relatives: An affected woman had a cousin that suffered from the same disease; his parents were cousins. His grandfather was married twice, and one of his daughters of the second marriage had nine children, of which two had phenylpyruvic oligophrenia. Fölling has observed in another marriage of cousins two children with phenylpyruvic oligophrenia. The author concludes that phenylpyruvic oligophrenia is a hereditary disease and that it is due to a single recessive gene. The characteristic mental retardation may sometimes be only slight and may even be overlooked for some time. In one case there was a discontinuous excretion of phenylpyruvic acid, and this patient was the one least affected mentally. Of the 34 patients, 33 had blue eyes and 31 blond hair. The muscles are often rigid, giving the patients a stooping posture.

WALLGREN, Stockholm, Sweden.

Diseases of Genitourinary Tract

FERTILITY IN CRYPTORCHIDS. CHARLES E. REA, Minnesota Med. **3**:216 (March) 1951.

The author studied eight patients who had had bilateral undescended testes and in whom orchiopexies had been done at least 10 years previously. All of these patients were clinically sterile, and four of the patients who submitted to testicular biopsy had an atrophic germinal epithelium. This author feels that the confusion in the literature as to fertility of cryptorchids operated on is due to the lack of differentiation between pseudocryptorchids and true undescended testes and that fertility of true undescended testes is not common. STOESSER, Minneapolis.

CONGENITAL HYDRONEPHROSIS AND TRAUMA IN LEGAL PROCEEDINGS. K. BENÍK, Pediat. listy **5**:108 (No. 2) 1950.

The paper deals with a case of supposed traumatic hydronephrosis. The patient, a 10-year-old boy, denied having any troubles before the accident, evidently because he had been told to do so by adults. There seemed to be no other reason for any other diagnosis than that of traumatic hydronephrosis. But the operation and a further close analysis proved it to be what is called by some authors congenital hydronephrosis caused by a valvule closing the ureter in its proximal portion. The trauma probably complicated this congenital hydronephrosis. The author points to the difficulty of an accurate diagnosis in such cases and to the probability of different points of view in determining the amount of the indemnity to be payed by insurance companies. The paper ends with a description of several cases of such congenital hydronephrosis, and the author urges a urological differential diagnosis of cases in which there is even slight suspicion.

FROM THE AUTHOR'S SUMMARY.

Diseases of Ductless Glands; Endocrinology

FACTORS IN THE RATE OF DEVELOPMENT OF VASCULAR LESIONS IN THE KIDNEYS, RETINAE, AND PERIPHERAL VESSELS OF THE YOUTHFUL DIABETIC. HOWARD F. ROOT, RICHARD H. SINDEN, and RALPH ZANCA, Am. J. Digest. Dis. **17**:170 (June) 1950.

Statistics are presented to show that in the young diabetic, premature vascular disease, nephritis, and retinitis are significantly commoner when his diabetes has been poorly controlled for 10 or more years than when it is fairly well controlled.

KIMBALL, Evanston, Ill.

EFFECT OF ADRENAL ENUCLEATION ON SERUM SODIUM. KATHARINE A. BROWNELL, FRANK A. HARTMAN, and RICHARD W. REIMAN, Endocrinology **47**:326 (Nov.) 1950.

Serum sodium concentration falls and remains below normal for a few weeks after adrenal enucleation, which removes a large proportion of the cortices, indicating that the tissue removed is necessary for maintenance of normal serum sodium concentration, the remainder being inadequate. That this is not due to glomerular zone insufficiency alone but involves other zones is suggested but not established by the data.

JACOBSEN, Buffalo.

INSULIN AND ADRENOCORTICOTROPIN LABELED WITH RADIO-IODINE. J. W. FERREBEE, B. B. JOHNSON, J. C. MITHOEFER, and J. W. GARDELLA, Endocrinology **48**:277 (March) 1951.

Evidence is presented to indicate that corticotropin (ACTH) and insulin may be labeled with radioactive iodine without loss of hormonal activity.

JACOBSEN, Buffalo.

SOME FACTORS THAT INFLUENCE THE RELEASE OF IODINE FROM THE THYROID GLAND. J. WOLFF, Endocrinology **48**:284 (March) 1951.

Variation in the release of I^{131} from the thyroid gland has been determined by means of external gamma-ray counts in rats subjected to a number of experimental conditions. In most cases I^{131} was injected 40 hours before the first count was made, and propylthiouracil treatment was then instituted to block further synthesis of organic iodine.

Effects of hypophysectomy, treatment with thyroxin, thyrotropin, and iodide are reported.

JACOBSEN, Buffalo.

PREVENTION AND REVERSAL DESPITE HYPERGLYCEMIA OF GLYCOGEN INFILTRATION ("HYDROPIC DEGENERATION") IN THE PANCREAS IN ALLOXAN DIABETES IN THE RABBIT. G. LYMAN DUFF and W. E. TORESON, Endocrinology **48**:298 (March) 1951.

Evidence here submitted makes it appear probable that hypoinsulinemia plays a more important role than does hyperglycemia in the pathogenesis of glycogen infiltration (so-called hydropic degeneration) in the islets of Langerhans, intralobular ductules, and centroacinar cells

of the pancreas of the alloxan diabetic rabbit. Insulin therapy, even though inadequate to control the symptoms of diabetes, may be partially responsible for the reported rarity of "hydropic degeneration" in the islets of Langerhans of the diabetic human subject.

JACOBSEN, Buffalo.

THE EFFECT OF ADRENALECTOMY IN THE RAT UPON THE RATE OF GROWTH OF TRANSPLANTABLE TUMORS. DWIGHT J. INGLE and BURTON L. BAKER, Endocrinology **48**:313 (March) 1951.

The data of these experiments show that adrenalectomy in the rat retards the growth of a transplantable carcinoma and of a lymphosarcoma.

JACOBSEN, Buffalo.

THE EFFECT OF HYPOPHYSECTOMY ON THE UPTAKE OF RADIOACTIVE IODINE BY THE THYROID OF THE RAT. RAYMOND V. RANDALL and A. ALBERT, Endocrinology **48**:327 (March) 1951.

Many investigators have demonstrated by means of I^{131} that the administration of thyrotropic hormone augments the avidity of the thyroid of the normal animal for iodine. On the other hand, little information has been forthcoming about the capacity of the thyroid to collect iodine in the absence of thyrotropic hormone resulting from hypophysectomy. Experiments here reported indicate that after hypophysectomy the rat thyroid collects about 12% as much iodine as before hypophysectomy.

JACOBSEN, Buffalo.

THE RELATION OF THE ADRENAL TO RED BLOOD CELL FRAGILITY. HERBERT MEGEL and ALBERT S. GORDON, Endocrinology **48**:391 (April) 1951.

The resistance of the blood to hypotonic lysis is increased after adrenal removal. This effect is not present when washed cells instead of whole blood is employed. The plasma is demonstrated to contain a factor(s) which inhibits hypotonic lysis.

JACOBSEN, Buffalo.

POTASSIUM DEFICIENCY AS CAUSE OF THE SO-CALLED RHEUMATIC HEART LESIONS OF THE ADAPTATION SYNDROME. ERNST PESCHEL, BERNARD BLACK-SCHAFFER, and CLOTILDE SCHLAYER, Endocrinology **48**:399 (April) 1951.

Selye found that severe overdosage with desoxycorticosterone acetate reproduces in the rat morphological lesions similar to those seen in periarteritis nodosa, malignant hypertension, and rheumatic fever. He concludes that these diseases are, at least partly, caused by an abnormal adaptive response of the adrenal cortex and represent diseases of adaptation.

It has been found that the addition of large amounts of sodium to a diet poor in potassium results in a more rapid loss of potassium. It is further known that desoxycorticosterone acetate increases potassium excretion.

The findings of the experiments here reported do not support the view that the heart lesions found in rats overdosed with desoxycorticosterone acetate have any connection with rheumatic fever or the adaptation syndrome. The pathologic and anatomic studies showed that the myocardial lesion is different from that of rheumatic fever and identical with that produced by potassium exclusion diets.

JACOBSEN, Buffalo.

A SYNOVIAL FLUID CLOT PREVENTION TEST FOR THE DETERMINATION OF HYALURONIDASE ACTIVITY. GEORGE H. WARREN and JANE G. DURSO, Endocrinology **48**:408 (April) 1951.

It has been shown that a mucinase which depolymerized the mucins of glandular and connective tissue was present in filtrates of cultures of Vibrio comma. This observation led to the development of a simple, practical test for the titration of mucinase. It was found that if a mucin solution was colored with Congo red and dropped into acid alcohol, an easily visible clot formed at the interface. In the absence of mucin the drop flattened out and left only a cloudy patch without a definite margin. On the basis of these observations, the authors have developed a synovial fluid clot-prevention test for the assay of hyaluronidase.

JACOBSEN, Buffalo.

OBSERVATION ON THE IN VIVO INACTIVATION OF TESTOSTERONE PROPIONATE BY THE LIVER OF THE WHITE RAT. JOHN T. GRAYHACK and WILLIAM WALLACE SCOTT, Endocrinology **48**:453 (April) 1951.

Pellets of testosterone propionate implanted in the spleen of castrate male albino rats failed to have an effect on prostatic weight when the rats were subjected to the following procedures, thought to affect liver metabolism: (1) carbon tetrachloride poisoning, (2) starvation for eight days, (3) hypophysectomy, (4) moderate inanition, and (5) a restriction of dietary intake to glucose and tap water only for 29 days. Under the same conditions pellets of testosterone propionate implanted subcutaneously always resulted in a marked increase in prostatic weight.

The persistence of this androgen-inactivating function in the face of liver toxins and dietary stress suggests that the mechanism by which the liver handles testosterone propionate differs markedly from that by which it handles estrogen. It is suggested from this remarkable persistence that the liver is a "physiological filter" for testosterone propionate and probably for other androgens. The intact normal organ probably has the ability to rid the body of many times the amount of androgen it is normally called upon to handle.

JACOBSEN, Buffalo.

ADRENAL INSUFFICIENCY IN INFANCY. LEO J. GEPPERT, WILLIAM A. SPENCER, and ALBERT RICHMON, J. Pediat. **37**:1 (July) 1950.

Geppert and his colleagues review the reported cases of adrenal insufficiency in infants and add one of their own. Their patient had vomiting, diarrhea, increased skin pigmentation, growth disturbance, hydrolability, and "crises" with febrile illnesses. He showed characteristic electrolyte changes, abnormal carbohydrate metabolism, and low ketosteroid excretion. Terminally irreversible hypoglycemia developed. Therapy with available whole adrenal preparations was only partially effective.

At autopsy only a trace of the zona fasciculata of the adrenal cortex was found. (The patient showed primarily a disturbance of carbohydrate metabolism.) The zona glomerulosa was present but diminished. (There was a relative stability of salt and water balance.) The zona reticularis was not present. (Accelerated growth of this patient when he was free of stress was attributed to elaboration of the "N" factor by multiple fetal cortex rests found beneath the capsule.)

The case is presented as the first of its kind reported in infancy that is not associated with intersexuality, the first to show primarily disturbance of carbohydrate metabolism, and the first with normal resolution of the embryonic cortex but incomplete development of the true cortex.

MACDONALD, Pittsburgh.

LATER STATUS OF JUVENILE DIABETICS. C. WILLIAM DAESCHNER, ROBERT W. DEISHER, and ALEXIS F. HARTMANN, J. Pediat. **38**:8 (Jan.) 1951.

The authors have obtained follow-up data on 120 children who had had diabetes prior to 15 years of age. Thirty are dead, the majority having died of acidosis. Data on 60 children who survived were carefully analyzed, and the results, in terms of progress and physical condition, make up the body of this report. The authors present evidence that the incidence of complications in diabetes is affected by the duration of the disease and the care exercised in its control. Good control may not entirely prevent the onset of degenerative vascular disease, but it may minimize its progress and thus prolong the useful life of the patient. One of the problems in the exercise of this control is that between the ages of 15 and 19 many diabetics become rebellious and uncooperative.

MACDONALD, Pittsburgh.

CARCINOMA OF THE THYROID IN CHILDREN: A TEN YEAR FOLLOW-UP. HUGH F. FARE and RICHARD NEWCOMB, Radiology **54**:401 (March) 1950.

This is a supplementary report, after a minimum of 13 years, on five patients (four girls and one boy) originally reported on in 1937. The boy (age 6 years) underwent surgery only; the four girls, both surgery and roentgen irradiation. Two were thought to have metastases in the lungs. One showed degenerative changes following 4,900 r (in air) to the thyroid region. All appeared to be well.

The authors concluded (1) that any nodular mass of the thyroid area in children should be considered malignant until proved benign by excision and biopsy; (2) that x-ray therapy is an important adjuvant to surgery, and (3) that distant metastases in these patients do not necessarily indicate an unhappy end-result.

ANSPACH, Chicago.

LATE RESULTS OF REMOVAL OF A PARATHYROID ADENOMA IN A CASE OF PARATHYROID OSTEOSIS. L. COURTY and G. LEMAITRE, Presse méd. **57**:1212 (Dec. 25) 1949.

The authors report the case of a patient with parathyroid osteosis who had been operated on 20 months previously. Not only had the general condition of the patient improved, with a normal mode of life resumed, but also the bony changes had largely healed, with disappearance of most of the bone cysts.

The authors have classified this as a case of osteitis fibrosa cystica.

DAFFINEE, Melrose, Mass.

INJECTION OF AIR INTO THE ANTERIOR MEDIASTINUM IN INFANCY FOR THE DIAGNOSIS OF THYMIC HYPERTROPHY. A. P. H. DEGOY and S. DIRIENZO, Presse méd. **57**:1215 (Dec. 25) 1949.

The authors describe in detail the technique of air injection into the anterior mediastinum and illustrate various types of thymic hypertrophy as revealed by this method.

DAFFINEE, Melrose, Mass.

CASE OF SYMPATHICOGONIOMA WITH MANY DIFFUSE SUBCUTANEOUS METASTASES. A. FERLAZZO, Lattante **21**:514 (Aug.) 1950.

An infant born with an enlarged liver and spleen and many subcutaneous tumors died at 8 days. Autopsy and histological examination revealed that the primary lesion was probably in the adrenal cortex; there were massive metastases to the liver and spleen. The tumor cells were undifferentiated and probably were sympathogonias.

HIGGINS, Boston.

DEFINITE DISTURBANCE OF BONY GROWTH: EPIPHYSEAL DYSGENESIS IN ATHYREOSIS AND HYPOTHYREOSIS. C. LOMBROSO, Minerva pediat. **2**:328 (July) 1950.

Lombroso uses the term "epiphysial dysgenesis" to designate the disturbances in osseous growth occurring in cretins and hypothyroid persons. Reports of 10 cases are given, with roentgenograms to illustrate the various clinical pictures found in this condition.

HIGGINS, Boston.

THYMOMA WITH ATYPICAL MANIFESTATIONS. J. LHOTÁK and F. PAVLICA, Pediat. listy **5**:103 (No. 2) 1950.

The authors describe a tumor of the thymus—a thymoma—in a child aged 2½ years. It was difficult to establish the diagnosis because of a right-sided exudative pleurisy. The microscopic examination revealed it as a lymphocytic tumor.

FROM THE AUTHORS' SUMMARY.

CHANGES IN THE CAPILLARY VASCULARITY OF THE HYPOPHYSIS IN THE HUMAN FETUS. KALEVI NIEMINEVA, Acta pædiat. **39**:315 (No. 4-5) 1950.

The author has investigated the development of the capillaries in the hypophysis of the human fetus during the latter half of the fetal period and made the following observations:

1. The volume of the capillaries in a unit of tissue increases in the latter half of the fetal period twofold in the pars distalis and fourfold in the neural lobe, owing to the facts that the length of the capillaries per unit of tissue grows in the former about 10 to 30% and in the latter about 40% and that the diameter grows in each by about three-fourths.

2. The ratio between the volumes of the capillaries of the pars distalis and the neural lobe varies in the specimens from 15:1 to 6:1. The ratio decreases during the fetal period.

3. The capillaries of the pars intermedia and pars tuberalis resemble those of the pars distalis.

4. In a newborn infant the density of the capillary network of the neural lobe is approximately the same as that in the cerebral cortex of the adult.

FROM THE AUTHOR'S SUMMARY.

OBSERVATIONS ON THE DEVELOPMENT OF THE HYPOPHYSIAL-PORTAL SYSTEM. KALEVI NIEMINEVA, Acta pædiat. **39**:366 (No. 4-5) 1950.

The writer found that the hypophysial-portal system is fully developed in human fetuses at term. About the middle of the fetal period, on the other hand, the capillary tufts essential to this system which penetrate from the sinusoids of the pars tuberalis into the region of the median eminence and the neural stalk are not demonstrable. As fetal life progresses, the formation of these vessel tufts can be seen.

It is concluded that if the hypothalamus regulates the function of the pars distalis by neurovascular channels, this regulation begins as late as toward the end of the fetal period.

FROM THE AUTHOR'S SUMMARY.

Diseases of Muscles, Bones, Joints, and Lymph Nodes

AMYOTONIA CONGENITA: REPORT OF THREE CASES WITH REVIEW OF LITERATURE. J. A. EPSTEIN, J. Mt. Sinai Hosp. **16**:137, 1949.

Epstein reports three cases of amyotonia congenita in two boys, aged 7 and 3 months respectively, and in one girl, aged 21 months. All three patients presented the usual atonia, absence of reflex responses, and immobility. The clinical course and the necropsy findings indicate that there is a congenital deficiency of the entire motor apparatus, from the cells of Betz of the precentral convolution to the motor end-plates and striated muscle fibers of the effector mechanism. The essential pathologic features include a diminution in the number of pyramidal cells in the third and fifth layers of the precentral gyrus, including absence or pronounced reduction in number of the giant cells of Betz. The usual grouping of the neurons in the ventral horns is absent. There is a paucity of cells, persisting only as occasional small, stellate, deeply staining elements with few processes. Cells resembling neuroblasts are present in both the cortex and the nuclei of the medulla and pons. The ventral roots are deficient in medullated fibers as compared with the normal number of myelinated fibers in the dorsal roots. This discrepancy is further evidenced in the cauda equina. Motor end-plates are present only on the muscle fibers of normal size and have never been observed on the small embryonic fibers which form the outstanding pathologic feature of the voluntary muscles. The diaphragm is the only striated muscle to retain its normal appearance. These observations, together with the absence of evidence of degeneration, inflammation, or gliosis, suggest that amyotonia congenita is due to a failure of development and maturation of the voluntary motor components of the central nervous system before neurotization of the skeletal musculature has been established. J. A. M. A.

SALMONELLA TYPHIMURIUM OSTEOMYELITIS. HOWARD S. TRAISMAN and GARDNER CHAMPLIN, J. Pediat. **38**:244 (Feb.) 1951.

Chloramphenicol (chloromycetin®) cured a patient with osteomyelitis caused by Salmonella typhimurium. This organism is rarely the cause of widespread osteomyelitis. This is apparently the first reported cure with chloramphenicol. MACDONALD, Pittsburgh.

INFANTILE CORTICAL HYPEROSTOSIS WITH INVOLVEMENT OF ILIUM. CLAY A. RACELY, JOSEPH B. BILDERBACK, and WILLIAM Y. BURTON, Northwest Med. **50**:418 (June) 1951.

The authors present a review of the literature to date of infantile cortical hyperostosis, discussing the pathology, clinical picture, differential diagnosis, and treatment. They present a detailed history of four cases from the Doernbecher Memorial Hospital for Children, two of which showed changes in the ilium not previously reported. The discussion presents specific

differential points between this condition and scurvy, disseminated bacterial osteomyelitis, syphilitic periostitis, vitamin A poisoning, and multiple bone malignancy. This excellent paper concludes wih a note of caution as to use of heroic and inherently dangerous therapy in what is a universally benign condition.

DOCTOR, Seattle.

CLOSING OF THE ANTERIOR FONTANELLE. MILTON R. AISENSON, Pediatrics **6**:223 (Aug.) 1950.

The age at which the anterior fontanel closed in 1677 infants varied between 4 and 26 months: in 90% of the infants it closed between 7 and 19 months. In the first year 41.6% became closed, 2.6% by the age of 6 months and 13.5% by the age of 9 months. Compared with data in older textbooks, this suggests a trend toward earlier closure of the anterior fontanel.

FROM THE AUTHOR'S SUMMARY.

CLINICAL STUDIES IN CRANIOSYNOSTOSIS: ANALYSIS OF FIFTY CASES AND DESCRIPTION OF METHOD OF SURGICAL TREATMENT. F. D. INGRAHAM, E. ALEXANDER JR., and D. D. MATSON, Surgery **24**:518 (Sept.) 1948.

Ingraham and his co-workers report 50 children with all varieties of premature closure of the cranial sutures for which the term "craniosynostosis" has been used. Twenty-nine children, 24 boys and 5 girls, presented premature closure of the sagittal suture. There were eight patients, five girls and three boys, with premature closure of the coronal suture, four patients with premature closure of the sagittal and coronal sutures, three with premature closure of the sagittal and lambdoid sutures, and six with closure of all cranial sutures. Twenty patients (40%), 7 of the sagittal group, 3 of the coronal group, and 10 with two or more sutures fused, were retarded to some extent before surgical treatment was practiced. Of the 44 patients treated surgically, 20 patients received treatment before the age of one year. Because of the rapid growth of the brain during the first year of life, it is to be expected that the best results from surgical treatment will be obtained during this period. This has been confirmed in the author's case. Many patients came to the hospital at ages varying from 3 to 7 years, and in these little was to be expected from any surgical procedure. In spite of this, there was definite improvement in the patient's behavior at home. Eleven patients (25%) showed retardation after operation. In general, the prognosis for mental development of a patient with premature closure of the cranial sutures treated under the age of one year is excellent, but if synostosis is evident at birth, surgical therapy should not be delayed more than a few weeks. Linear craniectomy, with polyethylene film inserted over the bone edges to retard regeneration of bone, has been adopted as the operation of choice. There have been no operative deaths, wound infections, or serious complications.

J. A. M. A.

ACUTE FULMINATING MYASTHENIA GRAVIS IN CHILDREN. D. L. A. BASTEDO, Canad. M. A. J. **63**:388 (Oct.) 1950.

Fulminating myasthenia gravis developed in a 10-year-old boy. Recovery was complete on treatment with neostigmine (prostigmin®) bromide. Only three of four cases in the literature have had such an onset. Attention is called to the advisability of trying neostigmine bromide in all cases of acute respiratory disease in which the nature of the causative factor is not fully established.

MCGUIGAN, Evanston, Ill.

OSTEOGENESIS IMPERFECTA PRESENTING WITH DELAY IN WALKING (TWO CASES). W. G. WYLIE and BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **42**:80 (Feb.) 1949.

The first case was of a boy aged 1 year 10 months who was brought to the hospital because of delay in walking. The second case was of a girl aged 2 years who also was brought to the hospital because of delay in walking. Data on all investigations, roentgenographic reports, and roentgenograms accompany the report. The family tree in the first case is also given, showing the father and two uncles to be affected.

WILLIAMSON, New Orleans.

POLYOSTOTIC FIBROUS DYSPLASIA (ALBRIGHT'S DISEASE). AHMED MINAISY, J. Roy. Egyptian M. A. **23**:785, 1950.

Osteitis fibrosa cystica (Albright's disease) is a syndrome which includes pathological fracture, limp, pain, and deformity of the affected limb. Precocious maturity may occur, as well as hyperpigmentation of certain areas of the skin. The disease must be differentiated from hyperparathyroidism, osteitis deformans (Paget's disease of bone), and dyschondroplasia (Ollier's disease).

McGUIGAN, Evanston, Ill.

TWO RARE HEREDITARY TYPES OF SKELETAL DYSTROPHIAS (GARGOYLISM AND MORQUIO'S DISEASE). N. NEIMANN and P. ARNOULD, Pédiatrie **37**:625 (Nov.-Dec.) 1948.

With two case reports the authors discuss the differential diagnosis of gargoylism and eccentro-osteochondrodysplasia (Morquio's disease). Both conditions are hereditary, appear during the first months of life, but in gargoylism, as contrasted to eccentro-osteochondrodysplasia, mainly the skull and face are affected, whereas the trunk is normal, the liver and spleen are enlarged, the cornea may be opaque, the intellect is below normal, and there is definite anemia. Roentgenography reveals a thickening of the cortex of the cranial bones in gargoylism but osteoporosis in eccentro-osteochondrodysplasia. The authors, contrary to statements in the literature, feel that these differential points are sufficiently characteristic to permit accurate differential diagnosis.

GLASER, Chicago.

THE SIZE OF NORMAL EPIPHYSIS OF THE FEMORAL HEAD IN THE CHILD AS SHOWN IN THE ROENTGENOGRAM. L. HOLLANDER, Helvet. paediat. acta **5**:484, 1950.

The area of the femoral capital epiphysis was measured in the roentgenograms of normal children. The relation to age, body weight, and height is statistically evaluated and shown graphically. The practical use of these charts is demonstrated.

FROM THE AUTHOR'S SUMMARY.

OSTEOGENESIS IMPERFECTA, WITH REPORT OF A CASE. N. G. MOJUMDAR and D. N. CHATTERJEE, J. Indian M. A. **12**:372 (July) 1950.

A case of osteogenesis imperfecta in a 6-month-old infant is presented, together with a brief description of the clinical picture and types of the disease.

McGUIGAN, Evanston, Ill.

MEDIAN FISTULA OF THE NECK COMMUNICATING WITH THE ANTERIOR SUPERIOR MEDIASTINUM. MARINO MINI, Clin. pediat. **32**:49 (Feb.) 1950.

Cases of fistulas of the neck connected with embryonal residues of the branchial apparatus or of the thyroglossal tract are numerous in the literature; we cannot say the same for fistulas of the neck connected with intrathoracic formations.

The author describes a case observed in a patient 20 months old; in the child six months previously corresponding with the jugular depression a pea-sized tumefaction had appeared and had increased slowly in size without causing any disturbances for three months. It then opened spontaneously, producing a fistula, which at the time was visible on the median line of the neck a little above the jugular depression. Fistolography showed a long tract which communicated with the anterior superior mediastinum, where it was connected with a shadow which was surely the thymus.

Since the child had few disturbances, he was not operated on, and he was dismissed with the instruction to return periodically.

The author endeavors to determine the nature and origin of the pathologic formation and examines the different diagnostic and etiopathogenetic suppositions; he proposes to classify it as congenital in origin, in reference to the permanence and the successive unfolding of residues of the embryonal thymus.

FROM THE AUTHOR'S SUMMARY.

CASE OF RETICULOSARCOMA OF THE LYMPH NODES. E. GRASSO, Minerva pediat. **1**:274 (July) 1949.

A girl of 9 years presented typical Mikulicz's syndrome and an increase in blood monocytes. The spleen and liver were not enlarged. Biopsies were made of a lymph node and the bone marrow. A diagnosis of reticulosarcoma was made.

HIGGINS. Boston.

ANALYTICAL STUDY OF THE GROWTH OF LONG BONES. G. COTELLESSA and A. DE MAESTRI, Minerva pediat. **3**:79 (Jan.) 1951.

Studies of the growth of the long bones of rabbits indicate that only 75% of the growth is referable to metaphyseal activity, while 25% is in the diaphysis itself.

HIGGINS, Boston.

CONGENITAL OSSEOUS LACUNA OF THE CRANIAL VAULT ASSOCIATED WITH A PIGMENTED NEVUS AND PARTIAL ATRICHOSIS. M. BELLONI, Pediatria **58**:220 (March) 1950.

A newborn girl presented a birthmark over the parietal-occipital region. Palpation over this area revealed soft tissue, although no tumor. A bone defect could be felt, oval in shape, 12 by 6 cm., confirmed by roentgenography. The condition is analogous to a spina bifida occulta. A possible etiological agent may have been a 20-day rheumatic infection in the mother during the third and fourth months of pregnancy.

HIGGINS, Boston.

BEHAVIOR OF TUBERCULOUS ALLERGY IN MALIGNANT LYMPHOGRANULOMA. B. NUNZIATA, Pediatria **58**:562 (July) 1950.

The tuberculin test should not be relied upon in making a differential diagnosis between malignant lymphogranuloma and other glandular diseases, especially those of a tuberculous origin.

HIGGINS, Boston.

ARTHRODESIS OF THE HIP. EDUARDO GOMEZ JAUREGUI, Bol. méd. Hosp. inf., México **7**:679 (Oct.) 1950.

The author reports eight cases in which arthrodesis of the hip was performed by Trumble's method as modified by Van Gorder; the mediate and immediate results were good. Of the patients, seven were children with coxalgia and the other an adult with hypertrophic osteoarthritis.

All the cases of coxalgia were diagnosed clinically, roentgenographically, and with the aid of biopsy of the iliac lymph nodes. In the painful cases a resection of the obturator nerve was done through the route of the biopsy. Alinement, as often as necessary, was carried out by casts, plain or skeletal traction, Soutter's operation, and, in one case, capsulotomy. Sutures were always done with cotton thread.

The technique of Trumble's arthrodesis as modified by Van Gorder does not frequently cause shock and leaves a wide visual field; if the great and lesser sciatic nerves are avoided, which is easily done, the risk is minimal; and the graft that is placed between the ischium and the femur, fixed to the latter with a bone lid and a screw, remains solidly in the place selected. The method reduces to a minimum the use of roentgenograms, which are quite necessary in Brittain's type of hip arthrodesis. The double team of surgeons reduces the time of operation, and when a frozen graft, or one preserved in thimerosal (merthiolate®) solution, is used, the trauma is diminished.

FROM THE AUTHOR'S SUMMARY.

EXTENSION OF LONG DURATION (DISTRACTION) IN THE TREATMENT OF CONGENITAL DISLOCATION OF THE HIP JOINT. R. PAVLANSKY, Pediat. listy **5**:215 (No. 4) 1950.

The nonoperative treatment of congenital dislocation of the hip joint sometimes leads to false reposition either below or behind the joint cavity, and this happens regardless of the method of treatment used—biochemical apparatus, plaster, or other. This position is always accompanied with a painful contracture which causes much suffering of the affected children. Previously these patients were left until operative reposition could be carried out. Nonoperative reposition

was in most cases unsuccessful, because the head always tended to return to the newly formed cavity behind or beneath the joint cavity and was fixed there by the muscle contractures. This happened mainly in cases in which the neck of the femur was in a valgus or anteroversion position. The author considered that improvement in these cases could be attained only by elimination of the contracture and therefore began to use extension of long duration (protracted extension). Good results had already been obtained in five cases in which the head had been squeezed behind or beneath the acetabulum. At the time of reporting there had been no failures. The same method was used to hold the head in position in two cases of osteomyelitis with empyema of the hip joint. The author is opposed to reposition of the dislocated hip joint under general anesthesia because of the trauma that occurs. Prolonged extension was therefore used in two such cases, and in both it was successful (one of the patients was a 2-year-old girl). In both of these cases it was not possible to bring about a relaxation of the muscles by the usual methods; the ultimate result was complete reposition, and not the slightest damage to the joint could ever be demonstrated. The treatment was then continued by the usual methods.

FROM THE AUTHOR'S SUMMARY.

HYPOPLASIA OF THE MANDIBLE AS A CAUSE OF RESPIRATORY DIFFICULTIES IN THE INFANT. STIG SJÖLIN, Acta pædiat. **39**:255 (No. 3) 1950.

Hypoplasia of the mandible in association with glossoptosis and often with palatoschisis is a not altogether unusual disease, often serious, and probably often overlooked. Of the two cases described here, the first one in particular is interesting. It shows the effect, in this case no doubt lifesaving, of a simple and logical therapy: the prone position and "orthostatic feeding."

FROM THE AUTHOR'S SUMMARY.

MYASTHENIA GRAVIS AND THE THYMUS: A SURVEY AND THE CASE OF A 9-YEAR-OLD GIRL. NILS TUNESTAM, Acta pædiat. **39**:395 (No. 4-5) 1950.

There is a definite connection between the thymus and myasthenia gravis, but the nature of this connection is a matter for discussion. In serum from patients with myasthenia gravis there is an element which, when injected into other persons, gives rise to myasthenic symptoms, owing to a neuromuscular block, which must probably be ascribed to a reduced synthesis of acetylcholine. The intimate dependence of the thymus on other endocrine organs renders it probable that myasthenia gravis is also influenced by them, above all by the thyroid gland and the adrenal capsules.

In myasthenia gravis remissions are often seen—as in cases of chronic polyarthritis—during pregnancy, a fact which ought to stimulate therapeutic experiments with cortisone acetate (compound E) or corticotropin (ACTH). In some cases, too, changes resembling those in encephalitis have been found in the brain.

The disease has been considered rare in children, but with increased diagnostic possibilities ever increasing numbers have been discovered and described. There are now reported between 20 and 30 cases among children under 10 years of age. (Three cases of transient myasthenia in newborn children of mothers with myasthenia gravis are excluded.)

After a survey of the clinical picture of the disease, a case in a 9-year-old girl is described in this case it first appeared with a morbid picture suggesting schizophrenia. After thymectomy about 10 months after the appearance of the first symptoms, she had almost complete recovery.

FROM THE AUTHOR'S SUMMARY.

LYMPHOGRANULOMA INGUINALE IN CHILDREN: REPORT OF 2 CASES. L. O. NYBERG and C. E. SONCK, Acta pædiat. **39**:433 (No. 4-5) 1950.

Nyberg and Sonck report on two new cases of lymphogranuloma venereum (lymphogranuloma inguinale) in young girls—13 and 14 years old—with severe rectal strictures. These are the eighth and ninth cases of lymphogranuloma venereum in children seen in Finland. Both children were probably infected by their mothers, who were suffering from the same disease with rectal manifestations.

FROM THE AUTHORS' SUMMARY.

CHONDRODYSTROPHIA CALCIFICANS CONGENITA. W. SWOBODA, Ann. pædiat. **175**:322 (Oct.) 1950.

The author gives a description of a case in which an isolated disturbance of the cartilage calcification (in the sense of a chondrodystrophia calcificans congenita in the tarsus) was detected roentgenologically in a newborn boy. These changes disappeared completely in the course of two years, but the child, who was under observation until the age of 4 years, retained in his face and in his body proportions signs of a slight chondrodystrophic growth disturbance.

After discussing briefly some of the peculiarities of this rare occurrence, Swoboda surveys the whole European and Anglo-American literature dealing with chondrodystrophia calcificans congenita. The observed case is considered to be a forme fruste, or abortive form, of the disease, and it is surmised that such forms occur more frequently, but fail to be diagnosed on account of the absence of marked external anomalies of the skeleton and of body growth.

FROM THE AUTHOR'S SUMMARY.

CHRONIC POLYARTHRITIS IN CHILDREN AND ITS GOLD THERAPY. BO S. V. BILLE, Nord. med. **37**:307 (Feb. 13) 1948.

Bille reports on 65 children, of whom 71% were girls, who were treated for rheumatoid arthritis during the period 1934 to 1947. In five cases the disease had followed rheumatic fever, in two cases scarlet fever, and in seven cases a trauma. Forty-three of the 65 patients received gold treatment. The injections were given once a week in increasing doses, and each course of treatment consisted of 6 to 10 injections. The initial dose varied from 5 to 40 mg. of gold, the highest dose being 20 to 150 mg., and the total amount for each patient was 100 to 1,000 mg. of pure gold, according to the weight of the child. Complications occurred in 53%, including skin and mucous membrane complications in 40%, blood complications in 12.5%, and slight irritation of the kidneys in 17% of the treated patients. In 84% there was an improvement: 58% of these showed substantial improvement.

WALLGREN, Stockholm, Sweden.

PES VARUS CONGENITUS. J. A. BÖÖK, Nord. med. **38**:1080 (May 28) 1948.

The author reports on the incidence of talipes varus in a population of 9,190 persons. Of 15 children of parents who were first cousins there were four siblings with clubfeet (26.6%). Among the 1,558 children of parents not related, there occurred 44 cases of clubfeet (2.9%).

WALLGREN, Stockholm, Sweden.

CASE OF OSTEOPETROSIS. ÅKE GYLLENSWÄRD, Nord. med. **41**:770 (April 29) 1949.

The author reports a case of osteopetrosis (marble bones). The patient was a one-year-old boy, birth weight 3,000 gm., who had been breast-fed for four months. His vitamin D supply was adequate. He had his first tooth at 6 months and sat without support at 10½ months. He could not yet stand without support. He had a tendency toward nasopharyngeal infections and suffered from anemia. Laboratory data were hemoglobin 48%, red blood cells 3,700,000, white blood cells 12,000 with normal differential count, and reticulocytes 3%. There were peculiar changes in the epiphyses. At roentgen examination typical osteopetrosis was found. There was an evident optical atrophy. One brother and the parents were healthy.

WALLGREN, Stockholm, Sweden.

CHONDRODYSTROPHY IN TWO SISTERS WITH NORMAL PARENTS. H. F. HELWEG-LARSEN and E. TRIER MÖRCH, Nord. med. **43**:180 (Jan. 27) 1950.

The parents of two sisters with chondrodystrophy were normal. The grandmother was short, 160 cm., with apparently too short legs and arms. Her brother was 162 cm. and his sitting height was 86 cm. The trunk and head were normal, the extremities too short. None of these two persons had typical chondrodystrophy. The author stresses that parents whose ancestors are short should not be unreservedly advised to have further children if they have had one child with chondrodystrophy.

WALLGREN, Stockholm, Sweden.

Diseases of Eye

RETROLENTAL FIBROPLASIA. A. L. EXLINE JR. and M. R. HARRINGTON, J. Pediat. **38**:1 (Jan.) 1951.

Exline and Harrington report on 80 infants who weighed less than 1,500 gm. at birth. Retrolental fibroplasia did not develop in any of them. These infants were given 5% dextrose in saline solution at 12 hours of age, and at 24 hours of age formula feeding was started. Vitamin C (cantaxin®) was given in increasing amounts up to 100 mg. daily by the fourth day. Vitamin D (drisdol®) administration was started at 7 to 10 days and was increased to 5,000 to 11,250 U. S. P. units by the age of 2 weeks. Some infants received small doses of iron ammonium citrate. No supplemental vitamin A nor vitamin E were used. Transfusions for hemoglobin levels below 10 gm. per 100 cc. were routine. All babies received vitamin K on admission. The authors do not attempt to explain the absence of retrolental fibroplasia in these infants but point out that excessive neonatal weight loss was avoided; no infants received high-potency water-soluble multiple vitamin preparations, or their vehicles; and none received liberal iron supplementation.

MACDONALD, Pittsburgh.

PENICILLIN IN THE PROPHYLAXIS OF OPHTHALMIA NEONATORUM. H. H. DAVIDSON, JUSTINA H. HILL, and N. J. EASTMAN, J. A. M. A. **145**:1052 (April 7) 1951.

Penicillin ointment was found to be less irritating and more bacteriostatic for use for newborn babies' eyes than silver nitrate, aqueous penicillin, or intramuscular injections of penicillin.

KIMBALL, Evanston, Ill.

RETROLENTAL FIBROPLASIA. HOWARD MALLEK and PETER SPOHN, Canad. M. A. J. **63**:586 (Dec.) 1950.

The authors discuss briefly the condition of retrolental fibroplasia. They point out that many of the patients studied had received transfusion shortly after birth and suggest an etiologic factor in transfusions.

MCGUIGAN, Evanston, Ill.

OPTIC NERVE COMPRESSION AND ITS DIFFERENTIAL DIAGNOSIS. S. P. MEADOWS, Proc. Roy. Soc. Med. **42**:1017 (Dec.) 1949.

The various effects on vision, visual fields, and optic fundi of optic nerve compression are described. Accessory methods of investigation and differential diagnosis are covered. Eleven cases are presented, with 17 figures.

HEARD, Monterey, Calif.

CONCOMITANT CONVERGENT STRABISMUS. D. O. CROMPTON, Clin. Rep. Adelaide Child. Hosp. **1**:204 (May) 1949.

Theories of etiology, typical case history, examination, and treatment of convergent strabismus are discussed. Attention is called to the importance of preventing amblyopia.

MCGUIGAN, Evanston, Ill.

CAPACITY OF SOME DRUGS TO PREVENT AN INDUCED EXPERIMENTAL EXOPHTHALMOS. R. PACHIOLI and G. CARDINI, Clin. pediat. **33**:145 (March) 1951.

In a recent article (*Clin. pediat.* **32**:439, 1950), Pachioli and Cardini reported a technique for producing exophthalmos without hyperthyroidism in guinea pigs by means of thyrotropic hormone and methylthiouracil. With this technique tests were done with the following drugs: testosterone, estradiol, desoxycorticosterone, ergotamine tartrate, choline, neostigmine (prostigmine®), and vitamin A—to ascertain if they would inhibit the production of the exophthalmos, Six guinea pigs were used in testing each drug. Choline and vitamin A were the only two of the drugs which prevented the appearance of the exophthalmos. Tests recently reported by Italian workers have shown that both choline and vitamin A will neutralize the effect of thyroxin on the basal metabolism of children.

HIGGINS, Boston.

STREPTOMYCIN TREATMENT IN PHLYCTENULAR KERATOCONJUNCTIVITIS. A. BONAVOLONTA and G. AURICCHIO, Pediatria **58**:539 (July) 1950.

Excellent results were obtained in the treatment of 20 patients with phlyctenular keratoconjunctivitis with streptomycin (0.02 to 0.03 gm. per kilogram of body weight daily for 30 days.).

HIGGINS, Boston.

Cutaneous Diseases; Allergy

STUDIES IN BACTERIAL ALLERGY: II. PREPARATION OF CRUDE NUCLEOPROTEIN AND POLYSACCHARIDE FRACTIONS OF BACTERIA. JAMES HOLMAN and OSCAR SWINEFORD JR., J. Allergy **20**:418 (Nov.) 1949.

A method is described for the separation of crude soluble nucleoprotein and polysaccharide fractions from a wide variety of bacteria.

HOYER, Cincinnati.

HOW FAR CAN WIND-BORNE POLLEN BE DISSEMINATED? S. SENIOR SACK, J. Allergy **20**:453 (Nov.) 1949.

A detailed account is given of the technique employed on vessels sailing between the United States and European ports and on four-engined planes flying between New York and Bermuda.

The findings would suggest that ragweed pollen can be transported in the atmosphere, under suitable conditions, a distance of at least 200 miles (322 km.).

HOYER, Cincinnati.

A TECHNIQUE FOR STUDYING THE NASAL ABSORPTION OF ALLERGENS IN HUMAN BEINGS. ROBERT A. CHAIT and MATTHEW WALZER, J. Allergy **21**:153 (March) 1950.

This study was made with 78 nonatopic adults. The upper outer aspect of the arm was sensitized to peanut antigen, with undiluted peanut extract, 1 : 4 dilution, and 1 : 10 dilution being used. The various concentrations were applied on a cotton pledget in the inferior meatus and middle meatus and on a 1-cm. square of purified cotton on the anterior inferior surface of the septum.

The antigen was absorbed from all three sites, as manifested by itching and urticaria at the sensitized skin site. The rate of reaction was essentially the same in the three locations. The 1 : 4 dilution was less painful than the undiluted extract, and the rate of absorption was slightly faster than with the 1 : 10 dilution. The rate of absorption from the septum was approximately as fast as that from the meatus. Application of the antigen was less difficult on the septum. With the recommended technique, absorption of peanut antigen from the septum was demonstrated in 33 of 34 subjects tested by the authors.

HOYER, Cincinnati.

ATOPIC DERMATITIS: I. AN EXPERIMENTAL CLINICAL STUDY OF THE ROLE OF INHALANT ALLERGENS. LOUIS TUFT, HAROLD S. TUFT, and V. MURIEL HECK, J. Allergy **21**:181 (May) 1950.

A case of atopic dermatitis in a man is reported. It was demonstrated that inhalation of house dust and Alternaria was the cause of the skin lesion. The case is reported to emphasize the importance of considering inhalant allergens in atopic dermatitis, especially in older children.

HOYER, Cincinnati.

SUDDEN DEATH DUE TO ALLERGY TESTS. M. COLEMAN HARRIS and NORMAN SHURE, J. Allergy **21**:208 (May) 1950.

A death occurring in a 25-year-old woman after intradermal tests is reported. Cottonseed allergen was believed to be the cause of the anaphylactic reaction. The pathological anatomy consisted mainly of acute pulmonary emphysema of the so-called guinea-pig type of anaphylactic reaction. The authors advocated the use of scratch tests preceding intradermal tests.

HOYER, Cincinnati.

NOTE ON THE TREATMENT OF DIAPER RASH WITH ALKYL-DIMETHYL-BENZYL-AMMONIUM CHLORIDES (ROCCAL). WILLIAM PFEFFER JR., and CLEMENT A. SMITH, J. Pediat. **37**:351 (Sept.) 1950.

Roccal® (containing 10% active alkyldimethylbenzylammonium chlorides) in a 1:5,000 dilution is an effective diaper antiseptic. It is nontoxic and inexpensive. Sixty-two of sixty-four cases of ammoniacal dermatitis cleared when diapers were impregnated with this solution after washing.

MACDONALD, Pittsburgh.

PURPURA FOLLOWING EXPOSURE TO DDT. FELIX E. KARPINSKI JR., J. Pediat. **37**:373 (Sept.) 1950.

In five children purpura developed after dichlorodiphenyltrichloroethane (DDT) sprays had been used in their homes. Four of the children had marked thrombopenia; three had nervous symptoms with irritability, impaired coordination, or clonic-tonic convulsions. All of these children recovered promptly without specific medication after change of environment.

MACDONALD, Pittsburgh.

RESPIRATORY ALLERGIES IN CHILDREN. LLYOD S. NELSON and ALBERT V. STOESSER. Minnesota Med. **33**:893 (Sept.) 1950.

The authors conclude that allergic diseases in the young child are frequently misdiagnosed. A careful history and detailed examination will reveal many cases of allergy which have heretofore been treated as recurrent upper respiratory tract infections. The frequent use of antibiotics for allergic children has been definitely abused. The value of antihistamine drugs in allergic rhinitis is discussed, and the authors conclude that antihistamines have limited value in asthma. Expectorant and bronchodilator drugs are best for the treatment of asthma.

STOESSER, Minneapolis.

TINEA CAPITIS. GEORGE GAETHE and FREDERICK GRIESHABER, New Orleans M. & S. J. **103**:256 (Dec.) 1950.

In 134 cases of ringworm of the scalp, cultures showed Microsporum audouini in 82.8%. M. gypseum was found in three cases, Trichophyton, gypseum group, in two, and T. sulfureum in two. Boys predominated six to one, and Negro children outnumbered white 124 to 10.

MCGUIGAN, Evanston, Ill.

INFANTILE ECZEMA. CHARLES KENNEDY, New Orleans M. & S. J. **103**:258 (Dec.) 1950.

The problem of eczema is very briefly discussed, with a routine for management outlined.

MCGUIGAN, Evanston, Ill.

CUTANEOUS MYIASIS IN INFANCY. SYDNEY ISRAELS and BEN SHUMAN, Pediatrics **4**:665 (Nov.) 1949.

Two cases of invasion of human skin by the larvae of Wohlfahrtia vigil (Walker) are described, and the literature of human myiasis in children is reviewed.

FROM THE AUTHORS' SUMMARY.

MERCURY POISONING FROM CALOMEL PRODUCING SUBACUTE ACRODYNIA AND ITS TREATMENT WITH DIMERCAPROL: REPORT OF A CASE. HUGH A. CARITHERS, Pediatrics **4**:820 (Dec.) 1949.

A 6-month-old girl had been given mercurous chloride in teething powders (a product called "Dr. Moffet's Teething Powders" commonly used in some areas of the United States) for two months before being seen with a chief complaint of photophobia. She was irritable, had flabby musculature, a maculopapular rash on the head, and slight hypertension and had lost weight.

She was given dimercaprol (BAL), the dosage being based on 2.5 mg. per kilogram of a 10% solution of the drug in peanut oil. Six doses were given daily for the first five days, three doses the sixth day, and two doses the seventh day. The total amount of the drug used was 0.86 gm. She became less irritable and gained weight; the rash cleared, but the photophobia persisted to a milder degree for a month after treatment.

Many of the signs observed in the patient suggest acrodynia. There were, however, no redness of the hands and feet, no excessive sweating, and no oral lesions.

FROM THE AUTHOR'S SUMMARY.

NEUROLOGIC COMPLICATIONS OF HERPES ZOSTER. A. R. NACHMAN, Pediatrics **7**:200 (Feb.) 1951.

Three cases of neurologic complications of herpes zoster are reported. In two cases there were meningeal reactions, and in one a motor complication (paresis of left leg). The latter is the first case occurring in a child noted in the literature. The relation of herpes zoster to varicella is discussed. Proof of the identity of the viruses causing those diseases depends on the identification of the infectious agents.

FROM THE AUTHOR'S SUMMARY.

AUREOMYCIN IN MOLLUSCUM CONTAGIOSUM. R. E. VOTTELER, Pediatrics **7**:206 (Feb.) 1951.

The response of a patient with molluscum contagiosum to aureomycin is reported. It is suggested that aureomycin therapy is a simple and atraumatic method of treatment of this condition for infants and small children.

FROM THE AUTHOR'S SUMMARY.

SOME THOUGHTS ON INFANTILE ECZEMA. ARTHUR R. BIRT, Canad. M. A. J. **61**:589 (Dec.) 1949.

A brief general discussion of the problem of infantile eczema is presented, with a short discussion of various theories as to its causation.

McGUIGAN, Evanston, Ill.

REPORT OF A CASE OF SWIFT'S DISEASE IN A CHILD AGED FIVE AND A HALF YEARS. DONALD CHEEK, Clin. Rep. Adelaide Child. Hosp. **1**:209 (May) 1949.

Acrodynia in a 5½-year-old girl is reported. Treatment and progress are not stressed.

McGUIGAN, Evanston, Ill.

A NEW TREATMENT OF FURUNCULOSIS WITH WHOLE LIVER EXTRACT. K. M. SUCKHTANKAR. Indian J. Pediat. **16**:153 (July) 1949.

The author treated 64 patients with furunculosis with injections of crude liver extract on alternate days. Beneficial results were observed in 48 cases, which the writer attributed to the effect of the liver in producing a marked cellular reaction with maximum phagocytic action. He also feels that the liver improves the general lowered tissue resistance and vitality which are sometimes thought to predispose to boils.

McGUIGAN, Evanston, Ill.

IMPETIGO FOLLOWED BY CHRONIC NEPHRITIS WITH AZOTEMIA AND LATER RENAL RICKETS. FONTAN and VERGER, Pédiatrie **37**:235 (March-April) 1948.

The authors report the case of a 10-year-old girl in whom acute nephritis developed after she had had extensive impetigo. She was hospitalized for two months and then discharged as cured. Two years later she was admitted to the hospital because of extensive genu valgum interfering with walking and standing erect. Physical examination and roentgenographic study revealed signs of rickets and retardation in statural growth. Urinalysis and blood chemistry studies showed the presence of chronic nephritis. Chemical findings of the blood were not characteristic of rickets, although the clinical and roentgenographic signs left no doubt as to the diagnosis.

GLASER, Chicago.

ACRODYNIA IN OLDER CHILDREN: ITS SERIOUSNESS AND TREATMENT BY ELECTRIC SHOCK. M. BERNHEIM and J. CONFAVREUX, Pédiatrie **37**:471 (July-Aug.) 1948.

Erythredema polyneuropathy (acrodynia) is a very rare condition in older children, but when it occurs it seems to take a much severer course. To the usual symptoms of erythredema polyneuropathy severe mental and emotional disturbances are added.

The case is reported of a 12-year-old boy who presented, aside from the classical signs of the disease, severe mental disturbances of somnolence, agitation with insomnia, hallucinations, and severe pains in hands and feet. All available treatment failed to show any signs of effect until electric shock therapy was instituted. After four shock treatments the child improved and finally recovered from all his physical, mental, and emotional disturbances.

The authors feel that the extreme disturbances of sleep point toward a diencephalic lesion which, it seems logical, would be affected by shock therapy.

GLASER, Chicago.

EPIDERMOLYSIS BULLOSA DYSTROPHICA IN AN INFANT OF 8 MONTHS. R. SACREZ, P. BEYER, R. BURGUN, and M. LAGOUTIERE, Pédiatrie **37**:623 (Nov.-Dec.) 1948.

An 8-month-old infant was born prematurely and had demonstrated bullous skin lesions ever since birth. Severe dystrophic lesions of the nails and swelling of the phalanges of hands and feet were present. Biopsy showed an atrophic epidermis and an abnormal basal skin layer. Autopsy showed toxic hepatitis and adrenal hypotrophy. A sister of the mother of the child and a sister of the child had died between 3 and 4 months of age, both presenting similar skin lesions.

GLASER, Chicago.

TREATMENT OF IMPETIGO IN CHILDREN. M. BALTER, Presse méd. **58**:300 (March 22) 1950.

Balter stresses three principles in the treatment of this common affliction of childhood: 1. Treat the underlying dermatitis which has become infected through scratching. 2 Prevent further spread of the impetigo. 3. Clean the impetiginous lesions, and apply suitable antiseptic lotions or ointments.

The author advises against the use of antibiotics, locally or generally. Classic methods of treatment, if properly carried out, will clear the condition as rapidly as do sulfonamides, penicillin, or tyrothricin, and with less danger of irritating the skin.

DAFFINEE, Melrose, Mass.

CASE OF SEVERE CONGENITAL ICHTHYOSIS. P. BRUSA and A. VERGA, Minerva pediat. **2**:352 (July) 1950.

A baby showed marked ichthyosis at birth; the child never did well nutritionally, and the skin lesions persisted until the child died at the age of 40 days. A postmortem examination is reported. The opinion is expressed that the origin of ichthyosis is traceable to an early malformation.

HIGGINS, Boston.

EHLERS-DANLOS SYNDROME. F. TOSCANO, Minerva pediat. **2**:497 (Oct.) 1950.

Two cases of Ehlers-Danlos syndrome are reported, one in a girl of 8 years and the other in a boy of 17 years. There was a family history of similar condition in both cases. There was hyperelasticity of the skin, especially over the knees and the elbows; areas of scarring and atrophy of the skin were present. Hyperelasticity of the ligaments was also found.

HIGGINS, Boston.

ANAPHYLACTOID PURPURA COMPLICATED BY ILEOILEAL INTESTINAL INVAGINATION. CARLOS HERRERA ROMERO, CARLOS SARINANA, and BIANCA PELIZZARO, Bol. méd. Hosp. inf., México **7**:724 (Oct.) 1950.

The authors report a case of anaphylactoid purpura in a 2-year-old boy; it became complicated by an ileoileal intussusception with an intestinal perforation caused by necrosis. An intestinal resection and a laterolateral enteroanastomosis were successfully performed.

FROM THE AUTHORS' SUMMARY.

THE INFLUENCE OF URETHAN ON ITCHING. ST. WOLFRAM, Wien. klin. Wchnschr. **61**:935 (Dec. 16) 1949.

Urethan in doses of 4 gm. a day diminished itching in various skin diseases. The ages of the patients are not given.

AMBERG, Rochester, Minn.

HYPERTRICHOSIS IN CHILDHOOD. A. HOLZEL, Acta pædiat. **40**:59 (Jan.) 1951.

Physiological hair distribution in infancy and childhood is discussed. A familial form of hirsuties is described. Transient hypertrichosis has been noted in cases of tuberculosis, celiac disease, marasmus, and acrodynia. Excessive hair growth in erythedema polyneuropathy (pink disease) and celiac disease has not previously been reported. A clinical classification of hypertrichosis in childhood is proposed.

FROM THE AUTHOR'S SUMMARY.

DERMATOMYOSITIS. ERIK J. HOLST, Nord. med. **38**:696 (April 2) 1948.

Holst reports two cases of dermatomyositis of unknown origin occurring in two girls, 8 and 10 years old. In the first case there were slowly progressive paresis, pain in the muscles, and edema of the face and the extremities. After universal light treatment, erythema developed in the face and the paresis became worse. After 3½ months of illness she was clinically examined. She died seven months after discharge from hospital. In the second case the child became acutely ill with fever and pain in several muscle groups. A tentative diagnosis of trichinosis was made. The muscle symptoms disappeared in the course of a few days, except for a remaining hard infiltration in the distal part of the flexors of the right arm. The child was given massage and exercise treatment, which increased the infiltration, and a flexure contracture arose. She was discharged from the hospital to be treated at an orthopedic clinic.

WALLGREN, Stockholm, Sweden.

SEASONAL VARIATION IN THE OCCURRENCE OF IMPETIGO CONTAGIOSA. EINAR SYLVEST, Nord. med. **40**:1926 (Oct. 22) 1948.

Analysis of the incidence in 508 cases of impetigo contagiosa showed a preference for the autumn. The disease was scarcely seen in infants under one year of age. The incidence was fairly constant in age group 2 to 13 years. Above the age of 30 the disease is extremely rare.

WALLGREN, Stockholm, Sweden.

STEVENS-JOHNSON SYNDROME (ECTODERMOSIS EROSIVA PLURIORIFICIALIS). JUSTUS STRÖM, Nord. med. **40**:1929 (Oct. 22) 1948.

Ström reports six patients, of whom three were children 2 to 3½ years of age, with ectodermosis erosiva pluriorificialis. The symptoms were typical. There was blood leucocytosis with deviation to the left. In two of the children the bone marrow was examined and was found highly reactive. Jaundice arose in one of the children. The course was mild in all cases. The author considers the disease to be an unspecific allergic syndrome due to various infections or agents with toxic action.

WALLGREN, Stockholm, Sweden.

EHLERS-DANLOS SYNDROME: CUTIS HYPERELASTICA. F. WIEGERS, Nord. med. **43**:304 (Feb. 17) 1950.

Two cases of Ehlers-Danlos syndrome are reported, one in a 5-year-old and the other in an 11-year-old boy with typical signs: hyperextensibility, hyperelasticity of the skin, and vascular fragility.

WALLGREN, Stockholm, Sweden.

Surgery and Orthopedics

SURGICAL MANAGEMENT OF BRANCHIOGENIC CYSTS AND SINUS TRACTS. CHARLES W. MCLAUGHLIN JR., Arch. Surg. **57**:450 (Oct.) 1948.

Branchial cysts are probably the commonest lesions to produce a single discrete and movable swelling in the lateral aspect of the neck. While congenital in origin, they usually appear in early

adult life. They occur as smooth, tense but mobile masses in the upper third of the neck anterior to the sternomastoid muscle. Fluctuation is usually demonstrable, but they do not readily transmit light. The exact embryologic origin of these defects is still not settled, but the principles of surgical therapy are well established. Six cases are reported in which the patients underwent surgical treatment without recurrences.

KAISER, Rochester, N. Y.

EXTREME HYPERPYREXIA IN SMALL CHILDREN AFTER BURNS. WOLFRAM KOCK, Nord. med. **43**:175 (Jan. 27) 1950.

A 3-year-old boy with severe burns was treated at the hospital in the usual way, with blood transfusions, controlled fluid and electrolyte balance, and local treatment. After two days the general condition deteriorated. His temperature was 42.3 C. (107.6 F.). His hyperpyrexia was treated by uncovering great parts of the surface of the body and by administration of salicylates. The temperature fell to 38 C. (100.4 F.); the boy improved and was discharged healthy. The author believes that the treatment of hyperpyrexia in this case played an important role in the healing.

WALLGREN, Stockholm, Sweden.

Teeth and Dentistry

ENAMEL EROSIVE PROPERTIES OF FRUIT AND FRUIT JUICES. CAREY D. MILLER, J. Nutrition **41**:63 (May 10) 1950.

Data given appear to justify the postulate that acid fruits generally have a slight enamel-erosive effect, in contrast to the marked effect of the juices made from them. Five tropical and semitropical fruits—namely, grapefruit, guava, Java plum, mango, and pineapple—and juices prepared from them have been fed to standard rats to determine their enamel-erosive properties. No adequate explanation for the different effect of fruit and fruit juice can be offered at the present time, but it appears not to be related to the titratable acidity of the two.

FREDEEN, Kansas City, Mo.

THE PREVENTION OF EXPERIMENTAL TOOTH DECAY BY TUBE-FEEDING. OWEN W. KITE, JAMES H. SHAW, and REIDAR F. SOGNNAES, J. Nutrition **42**:89 (Sept. 11) 1950.

The results of this experiment suggest that, with all other factors being controlled and equal, tooth decay is prevented in decay-susceptible rats when the direct effects of food in the oral cavity are eliminated.

FREDEEN, Kansas City, Mo.

THE EFFECTS OF FLUORIDE AND GRAPEFRUIT JUICE ON THE ETCHING OF TEETH. ARTHUR J. SPENCER JR. and LILLIAN N. ELLIS, J. Nutrition **42**:107 (Sept. 11) 1950.

The lower molars of young male rats were found to be strongly etched after the animals drank commercially canned grapefruit juice as the sole beverage during an 11-week period. The erosion was due to the acidity and not to the sugar content or any other factors, since no erosive action was found when sucrose-water or neutralized grapefruit juice became the fluid intake. There was about 60% protection when 50 ppm. of fluoride, as sodium fluoride, were added to the grapefruit juice.

FREDEEN, Kansas City, Mo.

THE PEDIATRICIAN'S RESPONSIBILITY IN THE PREVENTION OF DENTAL CARIES. GORDON H. ROVELSTAD, J. Pediat. **36**:687 (June) 1950.

Oral micro-organisms, acting on carbohydrates, produce localized acids which result in dental caries. A variety of factors influence this process, and no one of these factors can be named as the general cause of all dental caries.

Children should start periodic visits to an interested dentist at as early as 2½ years of age. Cavities in deciduous and permanent teeth should be filled. In addition, the child should learn to brush the teeth or rinse the mouth with water after every meal. Carbohydrates may be controlled by reducing the daily intake of refined sugars and soft starches and by eliminating between-meal and bedtime snacks containing these substances. Fresh fruits and green vegetables

may be given in abundance. Ammonium dentifrices may be valuable. Topical application of 2% sodium fluoride may be helpful; it cannot do harm.

MACDONALD, Pittsburgh.

PIGEON TOE AND ITS TREATMENT BY THE DENIS-BROWNE HOBBLE SPLINT. DOUGLAS G. MCKAY, Clin. Rep. Adelaide Child. Hosp. **1**:188 (May) 1949.

Use of the Denis-Browne splint in cases of pigeon toe is described briefly.

MCGUIGAN, Evanston, Ill.

PEDIATRICS AND PREVENTION OF DENTAL CARIES. GARCIA-GRASS, Acta pediat. españ. **88**:391 (April) 1950.

Garcia-Grass summarizes the role of the dentist in prophylaxis of dental conditions. He says, "The ancient concept of a dentist as one who pulls teeth and puts in artificial ones is to be substituted for a specialist in stomatology, nutrition, orthodontia, etc." The dentist must take an interest in all of these, and in the prevention of malformations, malocclusion, and caries.

Dental caries could be reduced more rapidly than many other disease conditions with proper care. This must be given by the dentist and must start with the pregnant woman. In his investigations at the National School of Puericulture (Child Care), Garcia-Grass reports a great cultural lag between the dentist's knowledge and public cooperation. Some mothers still believe, "A tooth is lost for each baby."

Grass urges that preschool children be examined regularly and be encouraged to eat proper food. The eruption of the six-year molars and the changes taking place in the dental arch of the child from 6 to 8 years should be watched carefully.

Besides emphasizing proper nutrition, the author recommends silver nitrate and fluorine where indicated, and the complete prohibition of candy and refined sweets for all children. Naturally he believes in regular dental inspection of school children and regular cleaning of the teeth.

ALLEN, Santa Fe, N. M.

Miscellaneous

PREVENTION AND TREATMENT OF MOTION SICKNESS. L. E. GAY and PAUL E. CARLINER. Bull. Johns Hopkins Hosp. **84**:470 (May) 1949.

Gay and Carliner report the results of their studies on the administration of dimenhydrinate (dramamine®).

During a 10-day sea voyage, dimenhydrinate was administered to 389 persons who suffered from seasickness. Of this number, 372 were completely relieved of symptoms within one hour after the first dose, of 100 mg. Seventeen persons derived only partial benefit or no relief. It was found that a dose of 100 mg. prescribed to be taken every five hours and before retiring was adequate to control the most distressing symptoms. When the patient was unable to retain a capsule, rectal administration proved effective. The benefit derived by this route was as rapid and as complete as that derived by the oral route. No untoward reactions to dimenhydrinate were encountered by any soldier who received the drug.

The action of dimenhydrinate on the prevention and control of motion sickness is not yet definitely established. Studies are in progress to attempt to explain the mechanism.

GUTTMAN, Wilkes-Barre, Pa. [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

NEWER INSECTICIDES AND SCABICIDES. C. J. LUNSFORD, California Med. **72**:350 (May) 1950.

Experimental and clinical data show that thiamine chloride taken internally protects against flea bites. Application of DDT powder to the breeding places of fleas controls infestation.

Clinical data appear to show that the use of an ointment containing gamma isomer hexachlorocyclohexane is an effective and pleasant means of treating scabies.

PRYOR, Redwood City, Calif.

SIMPLE INFANT TRANSFUSION KIT FOR OCCASIONAL USE. W. R. MACLAREN, California Med. **72**:453 (June) 1950.

A satisfactory infant transfusion set can be assembled on short notice from materials available in most offices. The required equipment: one 50 cc. syringe with adapter; one 10 cc. Luer-Lok syringe; one three-way stopcock (from lumbar puncture set); one set of disposable plastic intravenous tubing (Baxter or Abbott).

The advantages of this arrangement are that the parts are standard items of office equipment; they can be assembled in a few minutes, and returned to their ordinary function after use, and the use of disposable plastic intravenous tubing is inexpensive, and makes autoclaving and storage of rubber tubing unnecessary.

PRYOR, Redwood City, Calif.

MID-CENTURY WHITE HOUSE CONFERENCE ON CHILDREN AND YOUTH. HENRY F. HELMHOLZ, J. A. M. A. **143**:625 (June 17) 1950.

The mid-century conference has set the machinery in motion to enlist the participation of everyone in the 3,076 counties throughout the United States in determining whether its child health, educational, and welfare needs are met and its activities are adequate to help the child grow into a better, peace-loving citizen. The plans suggested seem complicated, expensive, and precarious for accurate achievement of results that can already be surmised.

Little mention is made of university research, or lack of it, or the development of practical techniques that can be disseminated among physicians, who are guiding the development of children by trying to teach families how to live.

KIMBALL, Evanston.

PITUITARY ADRENOCORTICOTROPIC HORMONE IN SEVERELY BURNED CHILDREN. FORREST H. ADAMS, ELDON BERGLUND, SAMUEL G. BALKIN, and TAGUE CHISHOLM, J. A. M. A. **146**:31 (May 5) 1951.

Three severely burned children were given corticotropin (ACTH). Its administration produced a decrease in fever, an increase in caloric intake, and an improvement in the emotional status. It did not interfere with wound healing or the take of skin grafts. It would seem that this adjunct to the treatment of severe burns needs further investigation.

KIMBALL, Evanston, Ill.

FAILURE OF ORAL ANTIPYRETIC DRUGS TO ALTER NORMAL HUMAN PAIN THRESHOLDS. R. R. SONNENSCHEIN and A. C. IVY, J. Pharmacol. & Exper. Therap. **97**:308 (Nov.) 1949.

Acetylsalicylic acid, aminopyrine, acetanilid, and acetophenetidin, in varying doses, were tested for their effects on normal human pain thresholds, determined by electrical stimulation of the tooth pulp. The effect of acetylsalicylic acid on the pain threshold of the skin was tested by a radiant heat technique.

In no case did a drug cause an effect on the pain threshold which differed significantly from that produced by a placebo.

These conclusions are drawn: 1. Any significant effect of the antipyretic drugs on normal human pain thresholds is due to a placebo effect, i. e., suggestibility. 2. Therapeutic efficacy in painful disorders is most likely due to the action of these drugs on the pathological process which secondarily causes the pain, or to some unknown mechanism.

PILCHER, Cleveland.

EFFECTS OF BAL ON TISSUE DISTRIBUTION AND EXCRETION OF MERCURY IN ACUTE MERCURY POISONING. J. R. FITZSIMMONS (BY INVITATION) and F. L. KOZELKA, J. Pharmacol. & Exper. Therap. **98**:8 (Jan.) 1950.

Four rhesus monkeys were given mercury bichloride and two of them were treated with BAL. After 5 days the animals were sacrificed and it was found that there was considerably less mercury in the kidneys of the BAL-treated animals, while most of the other tissues contained more mercury than was found in the untreated animals. Similar experiments were made on rats and it was found that approximately the same amount of mercury was excreted in the feces

of the two groups, but more mercury was excreted in the urine of the controls than in that of the BAL-treated rats.

The authors conclude, "It appears that BAL complexes the mercury in some innocuous form, preventing it from concentrating in the kidney, thus protecting that organ from damage and at the same time reducing the amount of mercury excreted by way of the kidney in a given period of time."

PILCHER, Cleveland.

REEVALUATION OF EFFECTIVENESS OF PENTAMETHYL-ENETETRAZOL (METRAZOL) AS ANALEPTIC AGENT DURING THIOPENTAL DEPRESSION. WALTER M. BOOKER, PEDRO A. MOLANO, DAVID M. FRENCH, and CECIL RHODES, J. Pharmacol. & Exper. Therap. **98**:207 (March) 1950.

The authors summarize the previous evidence, both experimental (in animals) and clinical, on the effect of pentylenetrazol (metrazol®) on thiopental sodium (pentothal®) poisoning. In experiments on dogs they conclude, and emphasize, that the effective dosage against the thiopental depression is proportionate to the depression, and is usually large.

Respiratory rate, per se, is not dependable in the evaluation of the effectiveness of pentylenetrazol. The respiratory rate may be increased with doses of pentylenetrazol that are inadequate to produce recovery, while further administration of pentylenetrazol may slow the rate, increase the amplitude, and shorten the recovery time. Oxygen saturation and blood pressure bear a definite relationship to these doses and results.

The pentylenetrazol dosage should not be given to the point of convulsions, which of themselves may increase the depression. These results will be very useful in the treatment of narcotic poisoning in man.

PILCHER, Cleveland.

AUREOMYCIN: IN VIVO AND IN VITRO OBSERVATIONS IN A CLINICAL LABORATORY. GEORGE E. FOLEY, HARRY SHWACHMAN, and H. B. MATTHEWS, New England J. Med. **243**:77 (July 20) 1950.

The successive strains of Staphylococcus aureus isolated from the nasopharyngeal cultures of eight patients with mucoviscidosis (pancreatic fibrosis), one patient with chronic osteomyelitis, and one patient with infected eczema exhibited eightfold to sixty-four-fold increases in resistance during aureomycin therapy. The strains from seven patients were studied in more detail by means of successive multiple single-colony fishings. The data derived from four of these cases suggest a gradual, orderly appearance of increasing resistance with prolonged in vivo exposure to aureomycin. The strains isolated from the lesions of a patient with infected eczema, on the other hand, showed a rapid increase in aureomycin resistance. The same strain exhibited a concurrent increase in penicillin resistance.

FROM THE AUTHORS' SUMMARY.

AN EVALUATION OF REPORTED POISONINGS BY ACETYLSALICYLIC ACID. LEON A. GREENBERG, New England J. Med. **243**:124 (July 27) 1950.

The author precedes a statistical evaluation of the reported poisonings by acetylsalicylic acid with a review of the effects of this widely used chemical on individual organs and functions of the body. It is evident that therapeutic doses of salicylates have no effect on cardiac action, respiration, acid-base equilibrium, renal function, hearing, or the clotting mechanism. These small doses may, in sensitive persons, cause gastrointestinal disturbances of a mild nature.

A review of the small number of cases of death from salicylate ingestion reveals that a large proportion of the deaths resulted from ingestion of amounts of the drug far in excess of accepted therapeutic doses, often in suicidal attempts. There were few, if any, instances in which, in the absence of allergy, the use of salicylates in therapeutic amounts had produced serious poisoning or death, even when this had been prolonged.

WHEELOCK, Denver.

SUDDEN AND UNEXPECTED DEATH IN INFANTS. C. G. GRULEE JR., New Orleans M. & S. J. **103**:243 (Dec.) 1950.

Various causes of sudden death in infants and children are discussed in clear and rational manner. Particularly good is the section in which the author disposes of the thymus legend

most effectively. Emphasis is laid on the likelihood of sufficient cause being found on careful postmortem examination. The author has contributed a calm and rational discussion which should be read and remembered.

McGUIGAN, Evanston, Ill.

PHEOCHROMOCYTOMA. NEIL N. LITMAN and DAVID STATE, Pediatrics **4**:735 (Dec.) 1949.

A case of pheochromocytoma is presented. The difficulties in establishing the diagnosis are stressed, and the following conditions are mentioned as having to be considered in a differential diagnosis: (1) renal disease; (2) coarctation of the aorta; (3) acrodynia; (4) lead poisoning; (5) Cushing's syndrome; (6) hyperthyroidism; (7) tumors of the hypothalamus; (8) essential hypertension.

N,N-dibenzyl-β-chloroethylamine (dibenamine®) was used in the diagnosis and in treatment; it was useful in controlling the hypertension, but its preoperative use was apparently ill-advised. Piperoxan compounds are helpful diagnostic aids, but tetraethyl ammonium chloride is of little value in establishing diagnosis or in treatment.

The patient received preoperatively digitalis, adrenal cortical extract, and saline solution. During surgery and immediately after the removal of the tumor, she received epinephrine and blood transfusions. Hypotension could not be counteracted, and she died.

The best surgical procedure is careful dissection with gradual clamping of the pedicle of the tumor in an effort to achieve stabilization of the blood pressure before extirpation of the tumor.

FROM THE AUTHORS' SUMMARY.

DOSAGE OF DRUGS IN INFANTS AND CHILDREN: I. ATROPINE. KLAUS UNNA, KURT GLASER, EARL LIPTON, and PAUL PATTERSON, Pediatrics **6**:197 (Aug.) 1950.

The susceptibility of apparently healthy children of all age groups to atropine by oral and subcutaneous administration was studied in carefully controlled experiments on 129 children. The minimum effective dose (MED) of atropine was determined by its effect in suppressing sialorrhea elicited mechanically by chewing gum and/or pharmacologically by subcutaneous injection of methacholine.

Variations in individual susceptibility to atropine are large in all age groups and independent of the route of administration (oral, or hypodermic).

The average per kilogram of MED body weight after oral administration is somewhat smaller in infants of 1 to 12 months and children from 12 to 36 months (0.16 and 0.14 mg. per kilogram of body weight respectively) than in older children in the age groups of 3 to 6 years and 6 to 12 years (0.22 and 0.20 mg. per kilogram respectively). Comparable results are obtained by hypodermic administration.

The ratio between the MED by mouth and the MED by hypodermic injection is approximately 3:1 in all age groups.

The determination of the susceptibility of children of various ages to atropine fails to adduce evidence supporting the assumption of an increased resistance to atropine or of a physiological vagotonia in infants.

The relation of the MED of atropine in apparently healthy children to the doses recommended in pediatric therapy is discussed. The calculation of the dosage of atropine by body weight is recommended.

FROM THE AUTHORS' SUMMARY.

BORIC ACID AS A POISON. E. S. YOUNG, R. P. SMITH, and V. C. MACINTOSH, Canad. M. A. J. **61**:447 (Nov.) 1949.

Six deaths in infants 6 to 11 days of age are reported which were due to accidental use of 2.5% boric acid solution in making the formulas. Extensive pathological and chemical studies are included.

McGUIGAN, Evanston, Ill.

SCORPION STING IN CHILDREN. K. C. CHAUDHURI, Indian J. Pediat. **16**:208 (Oct.) 1949.

One hundred sixty children with scorpion sting were admitted to the hospital over a period of 11 years. Eighty-five per cent of the children were removed against advice, not being

seriously ill. Thirty-two per cent of the remainder died. The clinical picture of collapse is similar to that seen in spider bites. Death is usually due to circulatory collapse. Treatment consists in administration of fluids, with calcium salts being given intravenously, plus specific antivenom if it is available.

McGUIGAN, Evanston, Ill.

PULMONARY MANIFESTATIONS AND DEATHS DUE TO THE INGESTION OF PETROLEUM PRODUCTS. S. SELBY and S. LEVIN, South African M. J. **24**:1040 (Dec. 16) 1950.

Petroleum products, namely kerosene, are responsible for a considerable number of hospital admissions in Johannesburg. One per cent of admissions were for this condition, or 29 in two years. There were two deaths. Twenty-eight cases were of children between 1 and 2 years of age; in the 29th case the child was 6 years. Lung changes occurred in 77%, many of whom had no clinical findings. Other symptoms in severe cases were severe toxemia, drowsiness, dyspnea, cyanosis, and tachycardia. Since many of these symptoms and signs are due to absorption of swallowed petroleum products, stomach lavage should be done as soon as possible.

McGUIGAN, Evanston, Ill.

COMMENTS ON POSOLOGY IN CHILDHOOD. J. DELPHAUT and R. BERNARD, Pédiatrie **37**:531 (Sept.-Oct.) 1948.

At the occasion of the appearance of new dosage tables for children the authors comment that the newer publications abandon the older methods of determining the dosage by age and permit greater flexibility and adjustability to the therapeutic indications in childhood.

GLASER, Chicago.

FATAL BELLADONNA-PHENOBARBITAL POISONING IN A 3½-YEAR-OLD CHILD. E. NAJMAN, Ann. pædiat. **176**:63 (Jan.) 1951.

Najman presents a case of poisoning with belladonna and phenobarbital in which the child was given 22½ grains (1.34 gm.) of phenobarbital and belladonna extract, 9 grains (0.54 gm.). The intoxication was discovered by the mother very late and treated unsuccessfully with 77 mg. of picrotoxin, 23 cc. of nikethamide, and 2 mg. of strychnine, which were given with an abundant supply of liquid by the enteral and the parenteral routes for 33 hours. In spite of the coma caused by the drugs, attacks of pertussis, which was the patient's original illness, occurred. The combination of phenobarbital and belladonna even in the largest (lethal) doses is thus ineffective and is barely able to mitigate the attacks, but not to suppress them.

FROM THE AUTHOR'S SUMMARY.

PASSAGE OF PENICILLIN THROUGH THE PLACENTA DURING PREGNANCY. E. GRASSET, H. DE WATTEVILLE, and P. DOSSENA, Schweiz. med. Wchnschr. **80**:841 (Aug. 12) 1950.

Fifteen women in different stages of pregnancy received an injection of 300,000 units of penicillin two hours before Caesarian section. Penicillin was transmitted from the sixth week of embryonal development to term. The concentration of penicillin in maternal and fetal circulation in the fetal organs and in the amniotic fluid shows that this passage is limited. Nevertheless, the concentration in the fetus is sufficient for an antibiotic action against micro-organisms sensitive to penicillin, and particularly against syphilis.

AMBERG, Rochester, Minn.

MICROELECTROPHORESIS AS CLINICAL METHOD. F. SCHAUB and A. ALDER, Schweiz. med. Wchnschr. **81**:483 (May 26) 1951.

A new apparatus for the electrophoretic determination of the serum protein fractions is described. For the determination 0.1 ml. of serum is sufficient. Interferometric recording replaces the "Schlieren" optio, and a thermostat is not necessary. A determination can be carried out by a technician in about one and a half hours. The apparatus is made by Firma Kern, Aarau, Switzerland.

AMBERG, Rochester, Minn.

FAVISM. G. CADEDDU, Ann. ital. pediat. **3**:302 (Aug.) 1950.

The author has studied the clinical, anatomicopathological, and histological aspects of eight cases of favism, and he has established the relations among the clinical symptomatology, the etiopathogenic interpretation, and the anatomicopathological reports.

FROM THE AUTHOR'S SUMMARY.

RARE ENCEPHALIC COMPLICATIONS IN TWO CASES OF FAVISM AND THEIR SIGNIFICANCE. G. CADEDDU, Ann. ital. pediat. **3**:337 (Aug.) 1950.

The author relates the clinical, anatomicopathological, and histological aspects of two cases of favism in which exceptional nervous symyptomatology, caused by an acute hemorrhagic encephalitis in the first case and by thrombosis of the longitudinal sinus in the second case, was added to the typical aspect of the disease. In both cases, since the hemoglobinuric favic symptomatology had already disappeared, the death was caused by encephalic lesions.

The author discusses the pathogenesis of these manifestations, and he believes that both may be determined, even if indirectly, by favism: in the first case, because of the deep alterations caused in the capillaries by a particular toxicity of the process which may have promoted the hemorrhage; in the second, because of the alterations of the colloidal state of the blood and the slackening of the circle which might have helped thrombosis.

FROM THE AUTHOR'S SUMMARY.

CHROMATOGRAPHY AND ITS CLINICAL APPLICATIONS. G. MAGGIONI and V. BACCHETTA, Arch. ital. pediat. e puericolt. **14**:171, 1951.

The authors give a condensed review on chromatographic technique, with special reference to paper partition chromatography and its most recent application to the clinical laboratory.

FROM THE AUTHORS' SUMMARY.

INTOXICATION FROM ATABRINE IN CHILDREN. GILDO NICHELE and CORMONS COSTANZI, Arch. ital. pediat. e puericol. **14**:221, 1951.

The authors have described four cases of poisoning from atabrine: the first patient showed catatonic syndrome with impairment of liver function; the second patient showed only impairment of liver function; for the third patient signs of polyneuritis have been recorded, and the last patient has shown polyneuritis and encephalitic syndrome.

In all four cases the presence of acridinic derivatives in the cerebrospinal fluid has been noticed; in the first two cases examination for urinary elimination of the acridinic bodies has been positive for about one month after the suspension of atabrine treatment, reaching a daily quantity between 8.4 to 2.7 mg.

The authors consider the syndromes as dependent on atabrine poisoning producing lesions of the liver tissues and of the other organs and tissues as a consequence of the enterohepatic circulation of the drug.

FROM THE AUTHORS' SUMMARY.

AEROSOL THERAPY IN INFANTS. C. TORRICELLI, Lattante **20**:385 (July) 1949.

Very satisfactory results were obtained with practically all of 75 infants with respiratory infections from aerosol therapy. For the very sick children antibiotics were also given parenterally. Procaine was added when penicillin was given by aerosol, except for patients with marked toxicity or liver disease. Streptomycin was used in cases of pertussis and proprietary ephedrine preparations in the cases of asthmatic bronchitis.

HIGGINS, Boston.

SULFONAMIDES GIVEN BY AEROSOL. C. IMPERATO and L. LANDUCCI, Lattante **21**:193 (April) 1950.

Observations with human and animal subjects were made to study the effectiveness and the safety of the aerosol method of administration of the sulfonamide drug sulfamethazine. The aerosol method was as effective as the oral in maintaining a sustained blood level of the drug.

No bronchial irritation or retention of the drug could be detected on postmortem histological examination of the lungs of animals killed after the aerosol administration.

HIGGINS, Boston.

USE OF LEONURUS CARDIACA IN PEDIATRIC THERAPY. E. ORLANDI, Lattante **21**:582 (Sept.) 1950.

Leonusina granulare, an extract of motherwort (Leonurus cardiaca), proved to be an acceptable sedative for 11 children; it lowered the heart rate and relieved anxiety and fear in the patients. The dose used was 0.03 gm. three times a day.

HIGGINS, Boston.

CAPABILITY OF THE INFANTILE ORGANISM TO SPLIT THE SALOL MOLECULE. P. SCHIAPARELLI and U. VIGNOLO-LUTATI, Minerva pediat. **1**:256 (July) 1949.

Determination of the amount of salicylic acid in the urine permits one to learn the quantity of phenylsalicylate (salol) which has been split in the intestine. Normal children 2 months to 12 years showed a splitting of 12 to 20% of the phenylsalicylate taken by mouth. Only five of 30 children ill with various respiratory or gastrointestinal disorders showed a splitting as high as 12%.

HIGGINS, Boston.

STREPTOMYCIN RESISTANCE AND PAS RESISTANCE. D. VUGA, Minerva pediat. **2**:170 (April) 1950.

Resistance of tubercle bacilli to streptomycin or to paraaminosalicylic acid (PAS) is not the only cause for failures from chemical therapy. The nature of the tuberculous lesion and the constitutional resistance of the individual patient are just as important.

HIGGINS, Boston.

700 DEATHS IN CHILDREN OF MEDICO-LEGAL SIGNIFICANCE. E. BOSSI, Minerva pediat. **2**:343 (July) 1950.

Of 11,000 medical-legal autopsies in Milan, 700 were on children. Of these 700 deaths, 112 involved neonatal deaths, 36 unexplained deaths in infants, 23 homicides, 2 suicides, 322 accidental deaths (only 85 from motor vehicles), and 195 deaths from disease. The cases in each group are analyzed, and there is a discussion of some of the more unusual cases.

HIGGINS, Boston.

POISONING FROM EATING THE BERRIES OF CORIARIA MYRTIFOLIA. L. CARTAGENOVA, A. GHIO, and A. AGNESI, Minerva pediat. **2**:600 (Dec.) 1950.

Coriaria myrtifolia is a plant with a purple berry which is found in the neighborhood of Genoa. Its poisonous ingredient is a glucoside whose toxic action is not unlike that of strychnine. The authors have seen 11 cases of poisoning in children who ate the berries. The main symptoms are convulsions, tachycardia, tachypnea (and Biot's breathing), and vomiting; there was no abdominal pain or diarrhea. All the patients recovered. The treatment included gastric lavage and administration of bromides, barbiturates, digitalis, and adrenal preparations.

HIGGINS, Boston.

HEPARIN ACTIVITY IN THE PLASMA OF NEWBORN AND OF NORMAL CHILDREN, AS DETERMINED BY TOLUIDINE BLUE. B. ANGELINI and E. GRASSO, Minerva pediat. **3**:147 (March) 1951.

The active heparin in the blood plasma of newborn infants was found to be about 30% higher than in the blood plasma of children and of adults. The analytical method of Meneghini and Cervini was used.

HIGGINS, Boston.

HYALURONIDASE IN PEDIATRIC PRACTICE. M. LUISA QUARTI and A. VERGA, Minerva Pediat. **3**:151 (March) 1951.

Seventy more or less dehydrated children were given by hypodermoclysis solutions of blood plasma, isotonic sodium chloride solution, dextrose, or amino acids, to which hyaluronidase had been added. Very satisfactory results were obtained, in that absorption was rapid; hypodermoclyses containing hyaluronidase give as quick and as satisfactory absorption as intravenous injections.

HIGGINS, Boston.

USE OF ANTIBIOTIC SPRAYS OR INHALATIONS IN PEDIATRICS. JOSÉ SELFA, Acta pediat. españ. **86**:143 (Feb.) 1950.

After reviewing the findings of Segal, Bryson, Kruege, and Barach on the use of penicillin by inhalation, the author reports further excellent results in a group of children suffering from bronchiectasis, chronic bronchitis, tracheitis, and asthmatic bronchitis which have been resistant to the usual antiallergic treatments. He found the blood levels as satisfactory as when the drugs were given by other methods and that none of the children showed toxic reactions or intolerance to the drug. For children who could cooperate he used an apparatus made in America, called "Premo," and for small babies, a special apparatus which, from the cut accompanying the article, is like an oxygen tent and respirator. For children with asthma of an allergic nature, he followed the treatment with vaponephrin,® a solution of 2.25% epinephrine hydrochloride in purified racemic form. This was further diluted to 1 : 100 and given by means of a spray or nebulizer.

The children with bronchospasm had this addition; there were only three of the 76 who needed it.

ALLEN, Santa Fe, N. M.

PEDIATRICS IN THE FIELD OF SOCIAL SECURITY: THE PROBLEM AND ITS SOLUTION IN PERU. MANUEL SALCEDO FERNANDINI, Bol. Inst. internac. am. protec. infancia **24**:76 (March) 1950.

In the Latin-American countries in which the economic, social, and sanitary conditions have not attained a sufficient development, it is advisable to carry out preliminary steps before an extensive plan of social security is begun. These steps can be summarized in the following points: the improvement of the sanitary level of the population; the extension of medical services until an adequate level is attained, and the introduction of allocations for family or subsidies for children in the form which best suits the socioeconomic situation of each country.

Peru being among the countries that are in this situation, it is believed that, as a start toward the solution of the problem, she must try hard to carry out the preliminary steps referred to above and train technical personnel in adequate number and quality to carry on that great work, the same as almost all Latin-American countries, in the field of public health and social welfare.

FROM THE AUTHOR'S SUMMARY.

NEED OF INCREASE IN TEACHING OF PEDIATRICS AND PUERICULTURE IN ARGENTINE UNIVERSITIES. PEDRO RUEDA, Bol. Inst. internac. am. protec. infancia **24**:157 (June) 1950.

From arguments presented the author draws the following conclusions: 1. The teaching of pediatrics and puericulture given in Uruguayan universities is not sufficient. 2. The biology of the child constitutes an autonomous whole from the physiological and pathological point of view, very different from that of the adult, and it demands particular dedication for its best protection and defense. 3. Consequently, it is necessary to augment the programs of pediatrics and puericulture to prepare the physician who must perform an important health mission in the country for his professional capacity.

FROM THE AUTHOR'S SUMMARY.

CASE REPORTS (AUTOPSIES). MAXIMILIANO SALAS MARTINEZ, ANTONIO VILLASANA ESCOBAR, JULIO CARRILLO RASCON, ARMANDO RICALDE GAMBOA, GUSTAVO LOPEZ POUMIAN, and P. DE M. LEONARDO HEIRAS ARZOLARZA, Bol. med. Hosp. inf. México **7**:901 (Dec.) 1950.

The authors report a case of septicemia caused by Salmonella typhi in a child 2 years 7 months old. There were evident lesions in the intestine, mesenteric lymph nodes, liver, spleen,

pancreas, and bone marrow. A second case is reported of primary virus hepatitis in a patient 3 years 9 months old. There was a marked destruction of parenchyma of the liver, which caused a serious insufficiency with a final comatose state. A case of hepatic zonal diffuse necrosis in a girl 12½ years old is presented. The disease caused jaundice, hemorrhages in several organs, and an extensive nephrosis, which in turn produced anuria and uremia. There was also a final bronchopneumonia.

A case of enterocolitis is presented. The patient was a 4-month-old girl. The disease caused malnutrition and dehydration; this last condition persisted for the last two weeks and was probably responsible for thrombosis of the upper longitudinal, right lateral, and lower longitudinal sinuses. There was final bronchopneumonia. Report is also made of a case of probable septicemia in a 2-month-old girl, with concomitant hemorrhagic infarct of the right lung, the right kidney, and the left adrenal gland. There was a final bronchopneumonia.

The last case was of rheumatic disease in a boy 12 years old. The joints and the heart were affected, causing pancarditis, which brought about a cardiac insufficiency that caused the death.

FROM THE AUTHORS' SUMMARY.

SUPRONAL (DE-MA) IN PEDIATRICS. LUDWIG SAUER, Arch. Kinderh. **137**:193 (Nov.) 1949.

Supronal, an improved sulfa preparation developed by Domagk, is a combination product of sulfathiourea, amino-methyl benzolsulfonamide, and sulfapyrimidin. This new preparation is practically free of any side reactions and can be given over a considerable length of time. It has a wide and intensive bactericidal action and is effective against anaerobic organisms. Daily dosage recommended is from 0.4 gm. per kilogram of body weight in infants, to 0.2 gm. per kilogram of body weight in children over 6 years of age.

ARON, Chicago.

NEUROBLASTOMAS IN THE CHILD. BAUZA F. DE CASTRO, and ELSA DE CASTRO, Rev. chilena pediat. **21**:397 (Sept.) 1950.

Two cases of neuroblastoma in infancy are presented. The evolution of the disease in both cases was somewhat unusual, as the diagnosis of malignancy was established by biopsy and yet both infants survived and are free of symptoms three and one half years after the diagnosis was established.

A thorough review of the present knowledge concerning neuroblastoma is given.

FROM THE AUTHORS' SUMMARY.

INTRAOSSEOUS-INFUSION THERAPY IN INFANTS. K. H. SCHÄFER and HEITHECKER, Kinderärztl. Praxis **16**:202 (July-Aug.) 1948.

It has been recognized that fluid-replacement therapy is of utmost importance in toxic nutritional disturbances. Technical difficulties of intravenous therapy in infants led the authors to try intraosseous therapy. After describing the exact technic of infusion in the upper third of the tibia or lower third of the femur, the authors present proof in table form of the effectiveness in diluting the blood stream in 13 infusions by the lowering of the hemoglobin content following therapy. Two complications occurred: One child had a bilateral osteomyelitis of the tibias where two transfusions each were given and an infection of the femur where no transfusion was given, evidently on a hematogenous basis. In the second case the injection was given subperiosteally because of an error in technic, but absorption followed moist applications and splinting.

GLASER, Chicago.

TREATMENT OF EXTENSIVE BURNS IN CHILDREN. H. RAMB, Deutsche med. Wchnschr. **76**:412 (March 30) 1951.

In the treatment of extensive burns in children, treatment and prevention of shock when necessary is first important. Then after the wounds are cleaned, sponges containing a strongly diluted penicillin solution are applied and fixed with a bandage of plaster of paris, instead of the formerly used pressure bandages. The plaster of paris bandages are kept on as long as possible, 8 to 12 days. Thirty-nine children were treated in the clinic, all with burns covering

15% of the body surface or more. The results were better than with previous methods of treatment. The author insists on having the children brought to the hospital as soon as possible without waiting for ointments or bandages to be applied. The burned parts are to be covered with some sterile cloth. Any ironed cloth taken from the closet will do.

AMBERG, Rochester, Minn.

UNEXPLAINED CASES OF SUDDEN DEATH IN CHILDHOOD. F. SCHLEYER, Med. Klin. **46**:166 (Feb. 9) 1951.

Three infants, 27, 43, and 56 days old, and one 7-year-old child died suddenly. Only the 27-day-old infant did not present any previous symptoms. Signs of asphyxiation were prominent at autopsy, and the possibility of asphyxiation by means of soft covering could not be entirely excluded. The other three children were manifestly ill, but the autopsy could not demonstrate any cause of death.

AMBERG, Rochester, Minn.

COELOM FLUID OF ASCARIS AS ANTIBIOTIC. H. M. JETTMAR, Wien. klin. Wchnschr. **63**:118 (Feb. 9) 1951.

Coelom fluid from Ascaris megalocephala and A. lumbricoides obtained without injury to the intestinal wall is strongly bacteriostatic for a group of micro-organisms. Some organisms, however, including those of the dysentery-Salmonella and the coli group are resistant.

AMBERG, Rochester, Minn.

ACUTE NITROBENZENE POISONING IN A CHILD. J. HNÁTEK and J. HOMOLKA, Pediat. listy **5**:47, 1950.

Acute nitrobenzene poisoning in a 2-year old girl is described. The clinical manifestations in children do not differ from those in adults. Emphasis is laid on the rapidity of the therapeutic action of methylene blue and on the negligible results from other forms of treatment. Nitrobenzene could be demonstrated in the blood, whereas no methemoglobin could be found.

FROM THE AUTHORS' SUMMARY.

TWO CASES OF THALLIUM POISONING. LARS-ERIK CARLGREN, Acta pædiat. **39**:438 (No. 4-5) 1950.

Two cases of thallium poisoning in children following the ingestion of rat poison are described. In such cases, treatment with cystine or dried yeast is worthy of trial.

FROM THE AUTHOR'S SUMMARY.

EXCHANGE TRANSFUSION AS TREATMENT IN POISONING. STEN AXTRUP, Acta pædiat. **39**:541 (No. 6) 1950.

A description is given of one case of chloramine poisoning and one case of aniline poisoning; both were in children whose lives were apparently saved by treatment with exchange transfusion.

FROM THE AUTHOR'S SUMMARY.

FETAL MOVEMENTS AND NERVOUSNESS. BERNHARD BESKOW, Nord. med. **44**:1443 (Sept. 8) 1950.

Beskow reports that 87.8% of the boys and 93.1% of the girls in a series of 1,127 children from infant welfare centers showed signs and symptoms of nervousness in the first months of life. The children often had a disturbing motor unrest, were easily irritated, and often very difficult to rear. They often screamed at night and during their later development exhibited frequently difficulties in adaptation, stubborn reactions, and other signs of nervousness. Inquiries disclosed that during fetal life these restless children had been more active than normal children. For 525 children, 320 boys and 205 girls, the mothers of 95% of the boys

and 89% of the girls considered that their children had been antenatally more restless than was normal. Only pluriparas had been included in the investigation. In a control series the figures were only 2% for boys and 3% for girls.

WALLGREN, Stockholm, Sweden.

PULMONARY SYMPTOMS AFTER DRINKING KEROSENE. J. J. SOER, Maandschr. kindergeneesk. **17**:118, 1949.

After drinking kerosene, three of four children showed pulmonic symptoms. On auscultation only a few rhonchi were heard, and these disappeared in a few days. On the roentgenogram, however, infiltration in the lower lobes from both hili were seen. In one patient the roentgenologic changes were already visible three hours after the drinking of the kerosene. The roentgenologic symptoms disappeared only after two to five weeks.

VAN CREVELD, Amsterdam, Netherlands.

SULFONAMIDE POISONING AND DEATH. THE SIE KIAN, Maandschr. kindergeneesk. **17**:190, 1949.

The author reports a case of death due to an allergic reaction in a 3-year-old boy who had been repeatedly treated for a dermatosis with small quantities of sulfonamides; the child died in consequence of eating 11 tablets.

FROM THE AUTHOR'S SUMMARY.

Society Transactions

SOCIETY FOR PEDIATRIC RESEARCH

Harry H. Gordon, M.D., President

Twenty-First Annual Meeting, Atlantic City, N. J., May 2 and 3, 1951

Third Session

Thursday Morning, May 3

Studies Concerning a New Inherited Abnormality of Hemoglobin. Dr. Eugene Kaplan, Dr. Wolf W. Zuelzer, and Dr. James V. Neel (by invitation), Detroit.

Through clinical, genetic, and physicochemical studies, a new inherited abnormality of hemoglobin has been recognized in American Negroes. The new hemoglobin can be separated from both normal and sickle cell hemoglobin by electrophoretic analysis. The structural anomaly of the hemoglobin molecule is determined by a gene inherited as a simple Mendelian dominant.

A distinct hemolytic syndrome which is intermediate between the benign sickle cell trait and sickle cell anemia results from the combination of the new hemoglobin with the sickle cell trait. In contrast to classical sickle cell anemia, this form of sickle cell disease is characterized by a mild hemolytic anemia with slowly progressive splenomegaly in the absence of cardiac or musculoskeletal manifestations. In vitro the erythrocytes sickle like those of sickle cell anemia. The bone marrow shows erythroid hyperplasia; fecal urobilinogen excretion is increased, and the survival time of the erythrocytes in normal recipients is shortened; but in the patients the red cell count and hemoglobin concentration are only slightly depressed. Reticulocytosis is slight, and icterus is not observed. Whereas in sickle cell anemia both parents are expected to have the sickling trait, only one parent of these persons shows sickling, while the nonsickling parent is a carrier of the new hemoglobin abnormality.

This abnormality when combined with structurally normal hemoglobin is expressed as an asymptomatic carrier state. The erythrocytes do not sickle but have a high incidence of target cell deformity and increased resistance to hypotonic saline. Although there is no evidence of hemolysis in such persons, their erythrocytes are eliminated with abnormal rapidity from the circulation of normal recipients.

The homozygous state with respect to this new hemoglobin has not yet been identified but may well be some already recognized atypical form of chronic hemolytic anemia.

Studies are now in progress to determine the incidence of this new molecular abnormality of hemoglobin.

DISCUSSION

Dr. Roland B. Scott, Washington, D. C.: Dr. Kaplan's paper was very interesting. I should like to ask him one point, namely, whether he has studied these variations of sickling in children of different ages. We have the feeling that age plays an important part in the sickling phenomenon. A few years ago we studied 262 newborn infants who presumably did not have sickle cell anemia but did exhibit sickling, and we found only 3.5% of these newborn infants to have sickling.

Studies of older children in the same city revealed a sickling incidence of about 7.5%. We have other data to indicate that age may influence the sickling phenomenon.

Dr. Shuman, New York: As Dr. Kaplan showed on one of his slides, there is a very striking resemblance of some of the cell curves to those found in Mediterranean anemia and similar genetically determined hemoglobin defects. I wonder, first, whether Dr. Kaplan has investigated hemoglobin in Mediterranean anemia, and, second, whether he has done anything about studying the alkali resistance of this new type of hemoglobin.

Dr. Eugene Kaplan, Detroit: The children in our group were not studied during their infancy; consequently, we have no information regarding differences in the rate or amount of

sickling with age in persons with the combination of this new type of hemoglobin and sickle hemoglobin.

Concerning Dr. Shulman's question relating to the Mediterranean syndromes, we have only the results of preliminary electrophoretic observations, which suggest that the new hemoglobin differs from the hemoglobin of Mediterranean anemia. Although the distinction between the cases thus far studied and the Mediterranean hemopathies, on the one hand, and true sickle cell anemia, on the other hand, is readily made on clinical, genetic, and hematological grounds, we feel that further experience may result in a greater overlapping of these syndromes, which may require exact chemical or immunochemical methods for differentiation.

Preliminary studies have revealed that the new hemoglobin is resistant to alkali denaturation. Studies are now in progress to compare this behavior with that of the alkali-resistant hemoglobins of Mediterranean anemia, sickle cell anemia, and sickle cell trait.

Congenital Familial Nonhemolytic Jaundice with Kernicterus: A New Clinical Entity. Dr. John F. Crigler Jr. (by invitation) and Dr. Victor A. Najjar, Baltimore.

Seven patients with congenital familial nonhemolytic jaundice with kernicterus are presented. This disease is manifested by marked jaundice appearing in the first few days after birth and persisting throughout life. Neurological signs of extrapyramidal disease become evident between 2 weeks and 3 months of age. Expressionless facies and a variable degree of rigidity of the musculature develop. Later the infants display distorted postures and show writhing movements characteristic of athetosis, although gross motor activity is reduced. Physical examinations are otherwise negative. The patients usually die of some secondary complication, frequently infection, in the first year of life.

A family pedigree of 505 persons revealed that all those known to be affected were third cousins and products of consanguineous marriages. The entity, therefore, represents a genetic mutation of a lethal recessive characteristic.

The only abnormal laboratory findings are the hyperbilirubinemia and the delayed excretion of injected bilirubin. The plasma bilirubin has ranged between 10 and 44 mg. per 100 cc., being most elevated in the newborn period when there were the superimposed causes of physiological jaundice. The bilirubin from these patients has been crystallized from the serum and found to have the same physical and chemical properties as indirect bilirubin. Four hours after the intravenous injection of 5 mg. per kilogram of commercial bilirubin into two of these patients, an abnormal retention of 23 and 40% was found. Results of other studies of the blood, including red cell fragility, reticulocyte counts, and bone marrow examination, studies of the urine and stool for bile and urobilin, and studies of liver function have been within normal limits.

Histological examination of liver from five patients has been made. In two of these the livers were normal; on one autopsy was performed at 17 days of age and on the other biopsy at 12 months of age. In the other three—for two biopsy was performed at 4 months of age and for one autopsy was performed at 10 months of age—there was some periportal scarring. The brain of the patient who died at 17 days of age was examined and showed the pathological changes characteristic of kernicterus.

The fundamental metabolic error resulting from this genetic mutation is unknown. A similar, usually milder type of jaundice described most frequently in adolescents and young adults has been called by numerous investigators Gilbert's disease, physiological hyperbilirubinemia, icterus intermittens juvenalis, constitutional hepatic dysfunction, and familial nonhemolytic jaundice. The latter term was used by Dameshek and Singer, who studied in some detail several families showing this abnormality. These persons seem to have a genetically determined specific hepatic dysfunction establishing an increased level of excretion of bilirubin without serious symptoms. The jaundice in our patients seems to result from a similar though more marked abnormality of liver function. A question still unanswered, but of great interest and importance, is whether the central nervous system involvement is a coexisting anomaly, a result of the same fundamental metabolic disorder, or secondary to the hyperbilirubinemia.

DISCUSSION

Dr. Richard L. Day, New York: This paper, so beautifully done, is extremely interesting to anyone who has been concerned with the kernicterus that develops in erythroblastosis. In

that disease also there is evidence of liver dysfunction, but it is hard to pin down, and it is nice to see that a liver disease which also has a large battery of normal liver function reactions is associated with brain disease.

The association between liver disease and brain disease has given rise to a large literature. I should like to mention a recent study made at the Psychiatric Institute in New York which bears on this. By a technique in which a cat's brain is isolated, so far as the blood stream is concerned, from the rest of the animal, it is shown that there appears to be some factor in the liver which is necessary to the glucose metabolism of the brain.

DR. WOLF W. ZUELZER, Detroit: I was very much interested in this paper because of our feeling that kernicterus does not depend on a specific immunological mechanism. It seems to result from a combination of circumstances of which we do not understand all the components. I was wondering if all the appropriate tests for isoimmunization against rare blood factors were done in these families. This is perhaps a foolish question to ask, because I am sure that has been done, and the genetic pattern was shown in a way that makes it unnecessary, but still, as we learn more about obscure and new factors, specific exclusion would seem desirable. One occasionally does see persons with erythroblastosis with very marked persistence of jaundice, and this picture resembled that.

One other question I should like to raise is whether or not the kernicterus seen at autopsy was a gross finding; in other words, whether there was actual staining or whether only histopathologic changes could be demonstrated. I believe the point was brought up a year or so ago at the meeting of this society that we should be very specific in the use of the word "kernicterus" and perhaps had better not use it as yet in a clinical sense until we understand the pathological process a little better.

DR. ROBERT J. MCKAY JR., Burlington, Vt.: I should like to ask Dr. Crigler what the national background of these patients was. Boston Children's Hospital has seen a number of patients from a particular area and from a particular national background. We saw a similar patient in Vermont this year who we thought was entirely separate, but on investigation the patient turned out to be from the same area and the same national background, namely, French.

DR. JOHN F. CRIGLER JR. (by invitation), Baltimore: I wish to thank the discussants for their remarks.

So far as testing in other members of the family was concerned, we have not done bilirubin excretion tests on them, but we have collected samples of sera for the determination of bilirubin levels. This has been done for the siblings and parents in two of the families, and no abnormality was found.

The pathological changes of kernicterus were those described grossly and consisted primarily of the staining of the basal nuclei.

The nationality origin of this group is German-English. They have been in the state of Maryland for some generations now, all having settled in one county.

Citrate Metabolism in Rickets and Tetany. HELEN C. HARRISON, PH.D. (by invitation) and DR. HAROLD E. HARRISON, Baltimore.

It is suggested that vitamin D influences the metabolism of citrate in the body and that this may be the basis of the antirachitic properties of vitamin D. This postulation is based on the following data:

The concentration of serum citrate in the postabsorptive state was found to be below the normal range in eight of nine cases of ordinary rickets. After administration of vitamin D in doses of 600,000 to 1,200,000 units, a progressive rise of serum citrate was found. In several cases the citrate concentration was raised above the normal range with subsequent return to normal. The rise of serum citrate paralleled other evidences of vitamin D effect and particularly roentgenographic evidences of healing of the bone lesions. In three rachitic infants studies of urinary excretion of citrate were made before and after treatment with vitamin D. In all three subjects an increased excretion of citrate in the urine was found after vitamin D treatment.

In a child with refractory rickets healing of the rickets did not occur until 150,000 units of vitamin D were given daily for approximately three weeks. Simultaneously with evidences of beginning therapeutic effect of vitamin D the serum citrate rose from an average of 1.8 mg. per 100 cc. to between 3.0 and 3.5 mg. per 100 cc.

A patient with polyuria, hyperchloremic acidosis, and hypophosphatemic rickets was investigated. The serum citrate was consistently low, ranging between 1.0 and 1.9 mg. per 100 cc. No change occurred after administration of 1,200,000 units of vitamin D. Healing of the rickets was achieved by the use of 40 cc. of molar lactate a day and 50,000 units of vitamin D daily. The serum citrate rose to values of more than 3 mg. per 100 cc. The urinary studies were remarkable in that the urinary excretion of citrate was extremely low (less than 5 mg. a day) and remained low despite the treatment with alkali and vitamin D.

Four infants with tetany occurring within the first 6 weeks of life were studied. No evidence of rickets was found. The concentrations of serum citrate were found to be low in all of these infants. Elevation of the serum calcium by a high calcium intake did not influence the serum citrate; after treatment with 600,000 units of vitamin D, the serum citrate rose along with a rise in serum calcium. Reduction of serum citrate has been reported in hypoparathyroidism, and it is possible that these findings in infants with neonatal tetany represent the effects of large doses of vitamin D on hypoparathyroid tetany.

A Modified Thyroid Function Test Using Radioiodine. Dr. Harold Nitowsky (by invitation) and Theodore Puck, Ph.D. (by invitation), Denver.

Tests of thyroid function, based on measurement of the accumulation of radioactivity in the gland following administration of I^{131}, have been described. A number of methods for estimating this accumulation have been employed, including measurement of the thyroid radioactivity with an external counter, analysis of the serum and urine, or a combination of these procedures. Error from several sources may impair the value of such estimates.

A method is described whereby the specific rate constant uptake of I^{131}, i. e., the thyroid iodide clearance, can be determined from measurement of the urinary excretion of I^{131} during the first 8 to 12 hours after administration of the tracer dose. Three to 10 μc of radioiodine give excellent results in children. The values attained are quantitatively reproducible, subject to less error than external measurements over the gland, and the procedure is convenient. Results of the tests in groups of euthyroid hyperthyroid, and hypothyroid subjects have shown good correlation with clinical evaluation of thyroid activity and with the estimates of I^{131} accumulation derived from analysis of urinary excretion over a 72-hour period.

DISCUSSION

Dr. William A. Reilly, Little Rock, Ark.: The results of the speaker are very similar to those which we have had for a good many years with this test.

One has to remember that iodine circulates in the blood stream and that iodine also is trapped by extrathyroidal tissues. Chaikoff, Morton, and Perlman, at the University of California, in 1931, proved elemental iodine in extrathyroidal tissues. Chapman and others in Boston showed, during the same year, that these extrathyroidal iodine depots had thyroxin-like compounds and activities.

What does all this mean in relation to my remarks? It means this—that I do not think one can use the urinary excretion test as an indirect measurement of thyroid gland uptake, as desirable as that test might be, as simple as it is and so easily carried out.

I still feel that the measurement over the gland is the best measurement of thyroid gland uptake. Its difficulties are relatively minor.

I was glad to hear the speaker bring out the point of the difficulties of gathering and measuring in the urine. I think we have to remember, then, that subtracting the amount in the urine from the total dose given does not mean that the remainder is all in the thyroid gland. There is about 5 to 10% in other tissues of the body.

Finally, there is an inherent error in running this kind of biological experiment; I think this amounts to about 5 to 10%.

Dr. Lee E. Farr, Upton, N. Y.: I should like to congratulate Dr. Nitowsky on his work. We have been doing a reasonable amount of iodine work at Brookhaven, particularly on patients with thyroid carcinoma. In those patients we have had occasion to follow the blood level and the iodine accumulation both in the metastases and in the urine. We have found that the measure of urinary excretion of iodine is probably the best single measurement of iodine uptake that is available.

There is one difference in the test we use from the one described today in that we use a 96-hour period of accumulation of urine and measure the total iodine excreted in that 96-hour period. For patients in whom we are doing thyroid function studies, we expect to find that the difference between the urinary excretion and the apparent in vivo accumulation, determined with use of calibrated counters, should be somewhere within 3 to 5%. I think the point Dr. Reilly raised is an important one, but, for practical purposes, I think one can safely use the urinary excretion of iodine as a measure of the uptake.

One should always bear in mind, however, that when iodine is given, and particularly when to a young child, radioiodine may have a carcinogenic effect, and if the information sought can be obtained in some other way, I think we should certainly make every effort to obtain it in that way, much as I think of the use of isotopes as a tool.

DR. HAROLD M. NITOWSKY (by invitation), Denver: I should like to thank Dr. Reilly and Dr. Farr for their remarks. The question that Dr. Reilly raises is, indeed, a pertinent one. The validity of the method of urinary assay, both our's and Dr. Farr's, is based on the assumption that the radioactive iodine which does not appear in the urine has been collected by the thyroid gland. We have found that by measuring the total quantity of radioiodine excreted in the urine and by measuring the radioiodine which is taken up by the thyroid, we can account for over 90% of any administered dose. When we can't do so, by close questioning of the patient we usually find that either a portion or a whole of a urine specimen has been lost.

Dr. Trunnell and co-workers at the Memorial Hospital have examined the distribution of radioiodine in various tissues of patients who came to postmortem examination. Although the old literature is replete with statements that selective uptake of iodine is found in organs such as the adrenal, the ovary and the pituitary, actually no selective concentration of the isotope in nonthyroid tissues was found by these investigators at the autopsy examination. On the basis of such evidence, we feel that the assumption upon which our analyses are based is a valid one.

The question of the difficulty in obtaining urine specimens has arisen at times with young infants. Fortunately, we have not had too much trouble with it. The youngest infant in our series was a 15-month-old boy, and it was possible to collect all the urine samples desired by tubing. By limiting the test to an eight-hour period, as we do, the possibility of ending with loss of urine is reduced considerably.

Hypertension in the Adrenogenital Syndrome Treated with Cortisone. DR. THOMAS H. SHEPARD (by invitation) and DR. SAMUEL W. CLAUSEN, Rochester, N. Y.

R. S., a patient with adrenogenital syndrome due to hyperplasia of the adrenal cortex, proved by biopsy, and with the clinically unusual feature of hypertension, was treated with cortisone acetate.

His accelerated growth and development began at 10 months of age. At 19 months he had pubic hair, penile enlargement, excessive musculature, and low-pitched voice. When he was studied at 2½ years, the blood pressure was 200/100, his height age was 5½ years and the bone age 10 years. Piperoxan and amobarbital (amytal®) sodium tests failed to lower the blood pressure appreciably. The 24-hour urinary 17-ketosteroids were 39.4 mg. The gonadotropins were less than 5 mμ per 24 hours.

Three months later at operation both adrenals were three to four times enlarged, and biopsy of the adrenals was done. The zona glomerulosa and zona reticularis were hypertrophied.

Twelve days postoperatively cortisone acetate administration was started. After the patient had received 40 mg. a day for 13 days, the blood pressure fell gradually to normal. Over a period of three and a half months the cortisone was gradually reduced to 10 mg. a day without return of the hypertension. The 17-ketosteroids were followed.

The adrenogenital syndrome may be due to excessive stimulation by corticotropin (ACTH). The hypertension is possibly on the basis of compensatory zona glomerulosa changes.

DISCUSSION

DR. EDNA H. SOBEL (by invitation), Cincinnati: We have had no experience with hypertension in patients with the adrenogenital syndrome. I was especially interested in the observation that corticotropin (ACTH) increased the 17-ketosteroid output. The recent work by

Dr. Albright and Dr. Wilkins suggested that the adrenals of these patients may not respond to corticotropin with increased 17-ketosteroid output.

DR. LAWSON WILKINS, Baltimore: I was exceedingly interested in this paper. I think one point that we should begin to recognize is that the congenital type of adrenal hyperplasia may present a number of variations in clinical picture: 1. The majority of the patients show manifestations of excessive androgen secretion with little evidence clinically of any involvement of the carbohydrate-regulating or the electrolyte-regulating function of the adrenals. 2. A fairly large group show deficiency of the electrolyte-regulating power of the adrenals in addition to excessive androgen secretion. 3. Recently, I have heard of one or two patients in whom there was failure of the carbohydrate-regulating function with a tendency to hypoglycemia. 4. Now we are seeing these patients that present the picture of hypertension, due possibly to a pressor effect or possibly to an excessive electrolyte effect of the adrenals.

We have had three patients of the hypertension type; two are sisters with the adrenogenital syndrome, and one is a small boy very similar to the patient just reported. It has been very striking that under cortisone therapy the fall in blood pressure occurred only when there was full suppressive effect on the adrenals, manifested by marked fall in urinary 17-ketosteroids. In one of these sisters, treated with intramuscular cortisone, the 17-ketosteroids dropped sharply, as in the case just shown, and her blood pressure fell immediately. The other sister, treated with oral cortisone, did not show full suppression, and her blood pressure did not fall at that time. When treatment was changed from oral to intramuscular cortisone, there was a sharp drop in 17-ketosteroids and, along with it, a fall of blood pressure.

I think that in such cases there may be some tendency for the blood pressure to rise again after a long period, because we do know that when an animal is hypophysectomized, the glomerulosa may actually eventually undergo some hypertrophy. It certainly does not undergo complete atrophy.

Just one word about the glomerulosa. I was very much interested to see in this case that there seems to be actually a hypertrophy of the glomerulosa zone. The patients with the salt-losing types of adrenal hyperplasia whose adrenals we have examined have shown a complete absence of glomerulosa. The one case of adrenal hyperplasia with hypertension in which we have examined the adrenal showed hypertrophy of the glomerulosa as in the case just reported. It all fits together very nicely.

DR. V. C. KELLEY (by invitation), Salt Lake City: I have one or two things I should like to say. One thing is that the author stated that the blood chemistry studies showed normal results with certain exceptions. I think it should be pointed out that that depends upon what in the blood is being studied; if you happen to be studying, as we are, such things as serum mucoproteins, polysaccharides, hexosamines, and hyaluronidase inhibitor, you find that the blood chemistry values are distinctly abnormal.

One point I should like to make (I am sure Dr. Wilkins will bear me out, because we have had some correspondence on it) is that, in the treatment of this condition, there is a great difference between the use of intramuscular and of oral cortisone. At Utah, Dr. George Sayers and I have had many conversations and done a great deal of thinking about this. We have done blood assays of corticotropin levels in a patient treated with cortisone and found high levels before treatment with those levels falling to normal immediately with the institution of cortisone treatment.

We have speculated in connection with Dr. Kendall's recent demonstration of the presence of a diene contaminant in his preparation of cortisone and, therefore, in the commercial preparation of cortisone, whether it is the diene contaminant that causes the repression of pituitary production of corticotropin and, therefore, the production of cortisone by the adrenal.

It seems possible, at least, since we now know there are these two different constituents present in cortisone as used clinically, that the difference between oral and intramuscular administration of cortisone may be due to the fact that one of the products is destroyed in the gastrointestinal tract or is not absorbed.

DR. NELSON K. ORDWAY, New Orleans: We have been observing recently a patient similar to the one presented who has, in addition, evidence of loss of salt. At the age of 3 months it was determined that, although he did not yet have virilizing tendencies seen clinically, there was an increase in the excretion of 17-ketosteroids. Studies have shown opposing effects on this

child of corticotropin and cortisone: namely, that there was a rise in 17-ketosteroid excretion on administration of corticotropin and a fall following the use of cortisone. Also, administration of cortisone caused salt retention in this child, whereas he lost salt and lost weight while he was receiving corticotropin.

I discuss this case only to point out the two-edged sword that we are dealing with in treating these infants with cortisone. We have just heard of several patients who have received cortisone and whose hypertension has been reduced thereby. Our concern at the moment with the infant we are following is that we have produced hypertension with cortisone, and at present we are reducing the dosage of the drug because of the blood pressure in this 8-month-old infant of 160/100.

Hemodynamic Studies in a Syndrome Resembling Malignant Hypertension Complicating Acute Poliomyelitis. Dr. Alex J. Steigman, Dr. William A. Brodsky, Dr. Walter S. Coe (by invitation), and Dr. Maurice M. Best (by invitation), Louisville.

There is little descriptive information available characterizing the hypertension and other autonomic changes in acute poliomyelitis. That hypertension is not coincidental is suggested from observations on 226 patients seen in a 1950 epidemic. A mean arterial pressure of 15 mm. Hg or more above highest "normal" for three or more days was the criterion used.

Severity of poliomyelitis is related to frequency of hypertension; it was found in 120 of 186 paralytic patients, but in only five of 40 nonparalytic patients. Age was not important: thus, there was hypertension in 50 of 82 paralytics 0 to 4 years old, 29 of 44 paralytics 5 to 9 years, 17 of 26 paralytics 10 to 14 years, and 24 of 34 paralytics 15 to 35 years. Hypertension appeared early in illness and was evanescent, usually was of under 14 days' duration.

Progressive hypertension developed in a 15-year-old boy with complete quadriplegia and involvement of the respiratory mechanism. There was no evidence of preexistent renal disease on admission in a normally developed boy. Initial mild hypertension of 130/90 has risen to levels of 230/160 nine months later. Although the respirator could be discarded less than two months after onset, there was no change in the quadriplegia with its resulting marked immobilization. By the fifth month, retinopathy and encephalopathy appeared, together with diminishing renal function. Attempts at characterizing the nature of the hypertension by cardiac catheterization revealed a normal output, markedly increased peripheral resistance, and no evidence of pulmonary hypertension. The findings did not simulate those of "neurogenic" hypertension as seen in dogs deprived of aortic and carotid innervation, in whom rate and output are elevated. Progressive skeletal demineralization was associated with hypercalcemia (12.6 to 18.0 mg. per 100 cc.) and hypercalcinuria, aggravating the hypertension. The use of an oscillating bed has not noticeably retarded the process.

Further attempts to characterize the nature of the hypertension were made by studying the effect of certain pharmacologic agents. No response on repeated trials was noted with piperoxan, N,N-dibenzyl-β-chloroethylamine (dibenamine®), dihydrogenated alkaloids of ergot, amobarbital (amytal®) sodium, tetraethylammonium chloride, and protoveratrine. Caudal anesthesia to a level of the sixth thoracic segment produced a fall in blood pressure from 200/150 to 120/80.

Encephalopathy, retinopathy, hypertension, renal damage, hypercalcemia, and nephrocalcinosis have appeared in patients with vitamin D intoxication and also after immobilization of portions of the body. Hyperparathyroidism has been thus simulated. The functional role of the parathyroids in this syndrome is not clear. When the factors of excess vitamin D and of immobilization can be removed, recovery has ensued, if permanent damage to renal arterioles had not occurred.

In the patient under investigation it is considered possible that a central nervous system lesion initiated hypertension with resulting arteriolar spasm, including the renal arterioles. Perpetuation of hypertension and its sequelae described above is considered to be associated with alteration in renal vasculature aggravated by urinary tract infection and hypercalcemia.

DISCUSSION

Dr. Milton Rapoport, Philadelphia: About six years ago Dr. Wallace McCrory and I studied a 10-year-old boy with extensive postpoliomyelitic paralysis, in whom hypertensive

encephalopathy developed. Respiratory paralysis and a complete quadriplegia had developed six weeks before his admission to the Children's Hospital of Philadelphia. The day following his hospital admission, he had convulsions while in the respirator. It was immediately recognized that the convulsions were hypertensive in orgin, and as a result of a series of observations made on this boy we arrived at a concept of the genesis of the hypertension which differs from that advanced by Dr. Steigman and his co-workers.

At the time of his convulsions his blood pressure was 160/100. His blood pressure was recorded as normal at the time of onset of his paralysis. Hypercalcemia was present—the serum calcium was 16 mg. per 100 cc. The serum phosphorus and phosphatase values were normal, and an assay of the serum parathyroid hormone content by the Hamilton technique showed no increase in circulating parathyroid hormone.

There was constant excretion of excessive calcium in the urine, as determined by the Sulkowitch test, and extensive demineralization of the skeleton was obvious in roentgenograms.

Reasoning from the fact that in immobilized patients demineralization of the bones occurs, we felt that the hypercalcemia in this boy was the result of renal inability to excrete the excessive quantity of calcium presented for excretion: A roentgenogram taken of the kidney showed a small degree of nephrocalcinosis. Glomerular filtration rate, measured by mannitol, was depressed to 50% of normal even though urinary concentration power and serum nonprotein nitrogen content were normal.

Feeling that we might interrupt the train of physiological derangements in this boy by doing something to interrupt the decalcification of his bones, we took him out of the respirator and subjected him to vigorous physical therapy many times daily. In four days his blood calcium had dropped to normal, and in one week his blood pressure had become normal.

With continued physical therapy the youngster maintained a normal blood pressure and normal serum calcium level, and the calcified shadows of his renal areas disappeared.

Blood and urine samples were obtained from 14 patients who were in tank respirators in the Philadelphia area at this time. Twelve of the 14 serum calcium values were in excess of 12.5 mg. per 100 cc., and the 14 single urine specimens all had excessive amounts of calcium.

While we have not observed the great number of patients that Dr. Steigman and his group have studied during the early days of poliomyelitis, we felt that our patient seen six weeks after onset with nephrocalcinosis and hypertension severe enough to cause encephalopathy had a completely reversible physiological defect. I should like to ask whether the rocking bed is completely adequate in the restoration of a positive calcium balance in a severely and extensively paralyzed patient or if more vigorous physical therapy is needed.

Dr. Lawson Wilkins, Baltimore: I was very much interested in this paper and particularly in Dr. Rapoport's remarks. I think this is a subject that should receive a great deal of attention.

I should also like to point out that with immobilization on paralysis decalcification of the bones occurs exceedingly rapidly and probably long before hypercalcemia is detected. I think it would be of very great interest to follow these cases from the beginning with the Sulkowitch test, as it is possible that there may be calcium deposition in the kidney long before renal function is impaired to the point that hypercalcemia would occur or before any nephrocalcinosis can be detected by roentgenography. I should be very much interested to see if one cannot spot the occurrence of a great deal of calcium release prior to that.

Dr. Lewis L. Coriell, Philadelphia: I should like to compliment Dr. Steigman on a nice piece of work. As he has indicated, hypertension is not uncommon in acute poliomyelitis, but not much can be done about it.

I should like to mention two respirator patients we saw last summer who had blood pressures over 160/100 two months after the acute illness. It so happened that both patients had severe acne along with their hypertension, and I should like to ask Dr. Steigman how often he saw this combination. The blood pressure in both patients responded to two measures which were taken. Transfer from the tank respirator to the rocking bed was followed by some improvement. Subsequently they were given 2-benzyl-2-imidazoline hydrochloride (priscoline®), and in both patients the blood pressure returned to normal or below. Severe dizziness after the first dose was noted in one patient. Reduction of the dose eliminated this side-effect, and a normal blood pressure was maintained on daily administration of 2-benzyl-2-imidazoline hydrochloride. These

results may have been entirely coincidental and unrelated to the treatment, and we wonder whether others may have made similar observations.

DR. JAMES ETTELDORF, Memphis: I should like to ask Dr. Steigman if he used magnesium sulfate on this patient. It seems that it would be rather apropos that it be used, in that hypercalcemia was present and considering the known antagonism that exists between these ions.

DR. JACK METCOFF, Boston: I am particularly interested in the use of caudal anesthesia in these circumstances, and I wonder if the authors happened to make any measurements concerning the changes in renal arteriolar tone.

DR. MITCHELL I. RUBIN, Buffalo: I should like to second Dr. Rapoport's remarks. I wonder whether one should label this patient as having malignant hypertension resulting from poliomyelitis, since the lesion probably results from immobilization in a patient with poliomyelitis. We have recently had two children with fractures, one a fracture of the lower thigh and the other a fracture near the pelvis. The speed of decalcification was rather remarkable. The decalcification was limited in a large measure, so far as the roentgenogram was concerned, to the immobilized extremity. If an arm or leg is immobilized, that extremity shows the greatest amount of decalcification.

This last patient of Dr. Steigman's had pyelonephritis, which could be a basis for primary renal damage. The large losses of calcium which occur in the immobilized patient with poliomyelitis, as Dr. Rapoport points out, could reasonably be expected to damage the kidney further. I wonder, therefore, Dr. Steigman, if this patient did not have renal hypertension which responded to caudal anesthesia.

Dr. Dodd and Dr. Rapoport reported a child who had a fractured leg, and who also later had hypertension with renal insufficiency on a similar basis. I think this condition is not considered frequently enough in immobilizing children.

DR. ALEX J. STEIGMAN, Louisville: One general comment before I take up the questions of the six discussants, to whom I am very grateful, and this is that since 1938 we have been very much interested in the effects of immobilization. Our attention has been drawn to a paper in *Lancet* with the very intriguing but deceptive title of "The Dangers of Going to Bed."

In 1938 we observed, although without benefit of the Sulkowitch reagent, how quickly in some children admitted to the Shriners' Hospital for Crippled Children in Philadelphia decalcification would begin.

Dr. Wilkins has raised the question of how early decalcification occurs. In this particular patient we spoke of, we observed heavy deposits of calcium in the urine three months before any hypercalcemia was detected and within six weeks of immobilization.

Dr. Coriell raised the point of acne, which he has observed in two patients. I don't know how often that happens to occur; we were intrigued with the possibility of a hypothalamic syndrome developing after poliomyelitis, in much the same way that we think of its developing or occurring after other forms of encephalitis. We were rather overanxious about acne and hirsutism last year and kept the endocrine laboratory busy determining 17-ketosteroids on a number of patients in whom hirsutism and acne seemingly developed, but we did not find anything we could associate with hypothalamic changes.

Dr. Coriell's question about 2-benzyl-2-imidazoline hydrochloride leads me to say that in 21 other hypertensive patients who were treated, in order to note the effect, with dehydrogenated ergot alkaloids, we did notice a definite and transitory drop in blood pressure which could be maintained so long as the patient was kept on dehydrogenated ergot alkaloids, which are believed to have a central effect.

Dr. Etteldorf raised the question of magnesium sulfate; it was used on this boy during the periods of hypertensive encephalopathy without any effect on the blood pressure. We used increasing doses.

I am sorry, Dr. Metcoff, we made no observations on arteriolar tone during caudal anesthesia and simply reported by the sphygmomanometer the blood pressure response.

Dr. Rapoport's and Dr. Rubin's questions, both closely related, I think, raise the whole question of what happens when patients are either completely immobilized in a tank respirator or immobilized for other cause. It may be recalled from the slide that this patient was kept in the tank respirator for as short a period as possible, I think approximately three weeks, and

then was gotten into a chest repirator as quickly as possible. It is because of this fear of the consequences of putting the patient to bed that we like to get patients into chest respirators and hence have access to their extremities at frequent intervals. This patient, in addition to having been treated on a rocking bed, which does not really move the skeleton very much, has had, by passive movement right from the beginning of his illness, a good deal of movement of the skeleton, and I think there may be a very large individual factor in how much immobilization will give rise to hypercalcemia and the sort of thing that Dr. Rubin referred to as having been reported by Dr. Dodd last year.

This is the kind of patient one occasionally sees in the crippled children's hospitals: with perhaps only one-quarter of the skeleton immobilized, the child is able to sit up, writhe around in bed, and move his other extremities, and yet hypercalcemia and increasing hypertension may develop. One wonders why there is such a great deal of variation and what the role of the parathyroid is.

Influence of Corticotropin (ACTH) upon the Growth of Premature Infants. Dr. William A. Silverman (by invitation), Dr. Richard L. Day, and Dr. Frederick C. Blodi (by invitation), New York.

In an effort to inhibit the progress of the proliferative vascular changes in the early stages of retrolental fibroplasia, we have had an opportunity to observe the effects of corticotropin (ACTH) administered to premature infants at the Babies Hospital.

Nineteen premature infants, born during the year Dec. 15, 1949, to Dec. 15, 1950, were treated with corticotropin. The ages of the infants under hormone treatment ranged from 15 to 84 days. The hormone was given in courses of 9 to 27 days, with doses varying from 1.7 to 20 mg. per kilogram a day. Five infants received second courses of corticotropin. Two patients died after the completion of therapy. Growth inhibition occurred during the course of corticotropin administration, and marked acceleration of growth was noted after cessation of therapy.

The average daily weight gains of the treated infants, calculated for comparable periods, before, during, and after treatment, were 24.9, 9.3, and 42.7 gm. a day respectively. Foreperiod daily gains were slowed immediately after the institution of therapy in all but the initial course of corticotropin given the youngest infant. This 15-day-old infant continued to gain weight at an expected normal rate while receiving 12 mg. per kilogram a day for 15 days. Moderate inhibition of weight gain occurred during the course of treatment using the smallest amount of corticotropin (1.7 mg. per kilogram a day for 19 days). Increased caloric intake during therapy failed to modify the inhibiting influence of corticotropin on daily weight gain.

"Rebound" increase in the rate of daily gain was noted after 22 of the 24 administered courses. The rate of daily gain doubled after cessation of corticotropin in the unaffected youngest infant and continued at this abnormal rate for seven days despite reinstitution of therapy 36 hours after the initial course was completed. For the last eight days of the second course, characteristic inhibition of weight gain occurred. In three instances, as the dose of corticotropin was lowered to 4.5, 4.6, and 7.1 mg. per kilogram a day, rapid increase in daily weight gain took place. After completion of 16 courses of corticotropin administered to 12 infants, the rate of "rebound" weight gain exceeded the foreperiod rate of gain.

Serial roentgen measurements of the length of the fibula were obtained at three- and four-day intervals in 12 of the 19 corticotropin-treated patients. In all but the one infant who received the smallest dose, growth in length of the fibula was retarded during therapy. Serial measurements of the occipitofrontal circumference of the head revealed changes in rate of growth during and after therapy that paralleled the fibular measurements.

The physical growth of presumably identical twins was compared. One twin received 11 mg. of corticotropin per kilogram a day for 20 days, a dose which resulted in characteristic growth inhibition; the co-twin received no hormonal therapy. The differences between the two infants in their physical dimensions were of the same order at the age of 10 months as they had been before therapy.

Postmortem examination of the two infants who died after completion of hormonal therapy revealed widespread pathological changes which included hypertrophied adrenals, hepatomegaly

with glycogen deposition in the liver, marked cardiac hypertrophy, calcium deposition in the renal tubules, and osteoporosis with irregularity and apparent deficient growth at the epiphyseal line.

DISCUSSION

DR. CLEMENT A. SMITH, Boston: We have had somewhat the same experience as has been reported, in terms of the growth changes, in our only patient that we followed very carefully, a patient of Dr. Olga Allers under treatment at the moment. I should like to use this opportunity to warn everyone that meddling with the endocrine function of newborn infants and premature infants with the more and more powerful tools which are becoming available does carry a considerable element of risk. The tools are being used for a very good purpose here but are sometimes applied for a less good purpose. In spite of certain inadequacies, as judged by adult physiological standards, premature infants and newborn infants are nevertheless normal for themselves. What is expected of them need not necessarily be that which is expected of the adult.

DR. SAMUEL Z. LEVINE, New York: Shortly I will present some work on the effect of corticotropin on some metabolic aspects and the clinical behavior of premature infants. When our group first undertook the study, we consulted with endocrinologists rather than with pediatricians, because of their greater experience in the field of corticotropin therapy. We were advised that if we were to get any results at all, we would have to use large doses; consequently, we started with the inordinately large dose of 50 mg. a day for premature infants weighing less than 2 kg.

While this work was going on, we had heard no repercussions of the deleterious effects that other institutions were getting with the use of corticotropin, so we happily continued in our course.

We have thus far treated a large number of premature infants, perhaps 20, with relatively large doses of corticotropin, and fortunately we have not encountered any of the catastrophies that have been reported.

It is interesting that, with respect to weight, we obtained precisely the same results as Dr. Silverman reports. However, if one summates the changes in the growth curve in the test periods with those in the after-periods, the rate of gain a day is almost identical with the foreperiod levels.

Similarly, the results that we obtained with height would indicate that the ultimate gain in height in a period of three, four, and five months after the course of corticotropin therapy is the same as that reported by Dunham in her book for premature infants of different heights and weights.

Obviously, the results that have been reported, as Dr. Smith pointed out, should serve as a caution to all who plan to continue the use of powerful hormonal agents.

DR. JOSEPH DANCIS, Flushing, N. Y.: We have also been interested in the use of corticotropin in the treatment of retrolental fibroplasia at Bellevue.

Dr. Lanman in our group has been following the effect on weight gain very closely. We have felt that we were able to minimize weight loss by increasing caloric intake. However, in view of the very unpredictable increases in edema of some of these children, it is a far less accurate index of growth than the one used by Dr. Silverman. We hope to check on this in the future.

With reference to the edema, a very interesting observation was made on two children. After the cessation of the use of corticotropin, which, incidentally, was used in very large doses similar to the one Dr. Levine used, we noticed a drop-off in edema, but after that there was a rapid accumulation of edema without there being a reinstitution of corticotropin, something that we find very curious at this point and incomprehensible to us.

In another two children we also noticed exophthalmos. It is rather difficult to measure, but those people who followed the children clinically were very well convinced that it was there during the use of corticotropin.

The pronounced general effect of corticotropin was that these children changed almost overnight into irritable and unhappy children such as everybody has observed.

In view of Dr. Smith's well-advised precaution about meddling with the endocrine status of newborn infants, it is with some hesitancy that I ask about this. We have discussed the possibility of effecting this delay in growth by introducing a second drug, testosterone. We have not done so, but I wonder whether anybody else has done so or considered it and what they thought about it.

DR. LAWSON WILKINS, Baltimore: Some of us in the audience are just a little curious to know about the retrolental fibroplasia. What happened to it?

DR. EDNA SOBEL (by invitation), Cincinnati: The interesting observations were made that actual cessation of growth was obtained with corticotropin in three infants. It is during infancy that children are growing at their most rapid rate. I wonder if this might not help to answer the question of whether the nitrogen loss seen in corticotropin therapy is catabolic or represents an antianabolic effect of the corticosterones which are produced in response to corticotropin. Dr. Silverman mentioned that an increased caloric intake did not prevent the impairment of growth. The remarkable degree of Cushing's syndrome which developed in the short period of 20 days makes one wonder whether an even higher caloric intake or a smaller dose of corticotropin might not have permitted growth to proceed.

If the growth inhibition should persist in spite of increased caloric intake, one would certainly think this suggests that corticotropin may be antianabolic rather than catabolic.

DR. W. E. LAUPUS (by invitation), New York: I should like to reiterate what has been said, with emphasis on the growth recession in these infants. It has been very striking and almost immediate with the institution of corticotropin therapy. We have thus far treated 13 infants who were at various stages in the pathogenesis of retrolental fibroplasia, and it is much too early, I think, at this time, to draw any definite conclusions as to the results obtained. However, it does seem somewhat promising.

DR. HARRY H. GORDON, Denver: I should like first to mention that if you give premature infants a diet that is adequate in calories, high in proteins, and low in fat, their rate of growth and their nitrogen retention will exceed that of full-term infants, and hormonal stimulation is unnecessary.

Concerning the point raised by Dr. Wilkins, namely, the effect of corticotropin on retrolental fibroplasia, it is difficult to get controlled observations which answer this question. The occurrence of retrolental fiibroplasia in any nursery leads to a considerable degree of hysteria. We feel that we do something of etiologic significance now that we didn't do 10 years ago, and when anybody comes along with a suggestion that a substance is of value in the treatment, it is difficult to restrict oneself to treating alternate patients.

If one has seen retrolental fibroplasia run its full course while corticotropin or cortisone are being given in large amounts, if one has seen the disease regress without any treatment at all, it becomes very difficult to feel certain about the value of hormonal therapy for retrolental fibroplasia.

I believe the contribution made by the Columbia group this morning might give us some reason for saying that we have here a mode of therapy potentially good but potentially dangerous that could be tested with adequate controls.

DR. WILLIAM A. SILVERMAN (by invitation), New York: I should like to thank all the discussants for their remarks and to reemphasize the dangers of prolonged corticotropin administration. We have reported only two deaths here, but in the total experience there have been six deaths. These infants became extremely debilitated and prone to secondary infection, and that accounted for most of the deaths. The concurrent use of antibacterial agents would certainly seem wise.

Dr. Dancis' remarks concerning edema are interesting. We have not restricted salt in these infants. They received the usual rations. Edema has been seen infrequently and then transiently at the end of the first week of therapy. We have seen no example of this reaccumulation of edema upon cessation of therapy. However, the report of exophthalmos during therapy interests us because we have noted bulging fontanels after withdrawl of corticotropin which we could not explain.

In partial answer to the suggestions of Dr. Dancis and Dr. Sobel concerning testosterone, we have administered methylandrostenediol and corticotropin concurrently and noticed no effect on the inhibiting influence of corticotropin.

I should not like to enter into the retrolental fibroplasia discussion. Dr. Day will discuss that later.

News and Comment

PERSONAL

Appointment for Dr. U. Pentti Kokko.—The University of Louisville School of Medicine announces the appointment of Dr. U. Pentti Kokko as Associate Professor in Child Health Research. Dr. Kokko will continue studies in poliomyelitis in the school's Kentucky Child Health Foundation Laboratory, which is under the direction of Dr. Alex J. Steigman, Professor of Child Health.

Book Reviews

Asphyxia Neonatorum. By William F. Windle, Ph.D., Sc.D. Price, $2.00. Pp. 70, with 8 figures and 4 tables. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1950.

This short monograph deals with the fundamentals of developmental physiology pertaining to respiration. It begins by describing the fetal-maternal relationships in the developing placenta, then discusses the characteristics of the blood of the fetus and of the newborn, the fetal circulation and the changes that take place at birth, and the conditions of intrauterine respiration, such as blood flow through the placenta, oxygen consumption and cardiac output in the fetus, blood pressure and vascular reflexes, fetal hemoglobin and oxygen capacity of fetal blood, and oxygen content and saturation of fetal blood. Fetal respiratory activity and the mechanisms involved in the initiation of air breathing together with experimental evidence are concisely discussed and summarized. Finally the results of asphyxia are considered, not only in relation to fetal and neonatal death, but also in regard to the effects upon brain tissue and the resultant handicaps in the lives of those who survive asphyxia at birth.

The importance to the practicing physician of a better understanding of fetal physiology becomes increasingly apparent. The welfare of the fetus and of the newborn depends greatly upon it. The author is a pioneer in the field of fetal physiology. His monograph is a clear and concise discussion, epitomizing present knowledge of the factors concerned in fetal and postnatal respiration. Every physician responsible for the welfare of the fetus and of the newborn needs this knowledge, and this little book furnishes it in an interesting and concise style and is authoritative.

Teaching the Retarded Child at Home. By Edna Davidson Osterhout, B.A. Price, $2.50. Pp. 67, with more than 35 unnumbered illustrations. Seeman Printery, Inc., Durham, N. C., 1950.

The author is a teacher of handicapped children at the Brett School, Dingman's Ferry, Pa. A preface by Dr. W. C. Davison, Professor of Pediatrics, Duke University School of Medicine, states that there are nearly one million mentally retarded children in the United States. Many are tragic "in-betweens" who are not quite eligible to enter special schools but are also not so retarded that they have to be committed to institutions for the feebleminded. These children have the ability to learn, however slowly, and the purpose of this book is to bring teaching to these handicapped children at home.

The book has been planned so that home teaching is available without extra expense for equipment or materials or any specially trained teachers. It includes exercises in reading, writing, spelling, and arithmetic and also lists a number of special magazines, and books appropriate for these handicapped children. It is a step forward in an attempt to educate the great majority of unfortunates for whom, as Drew Pearson has stated, the expenses of a private school cannot be afforded and who roam the streets because their parents are afraid to expose them to the ridicule of other children and since there is no place for them in the usual school programs.

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*References:

1. Stokes, J., Maris, E. P., and Gellis, S. S., The Use of Concentrated Normal Human Serum Globulin (Human Immune Serum Globulin) in the Prophylaxis and Treatment of Measles. J. Clin. Invest. 22:531-540, 1943.

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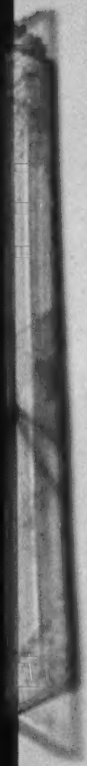

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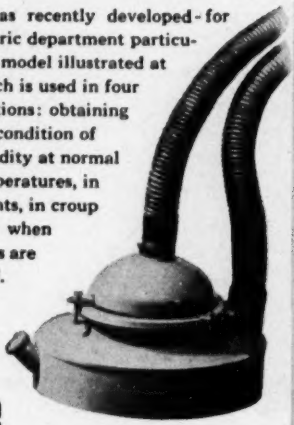

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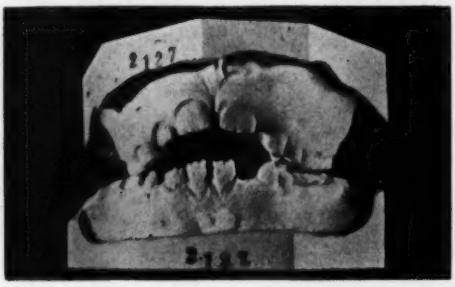

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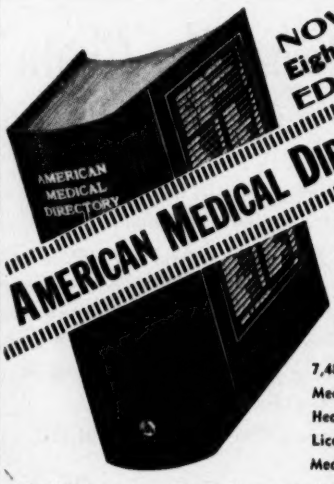

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1. Bruce, J. W., Hackett, L. J. and Bickel, J. E.: Feeding Premature Infants, J. Pediat. 35:201 (Aug.) 1949.

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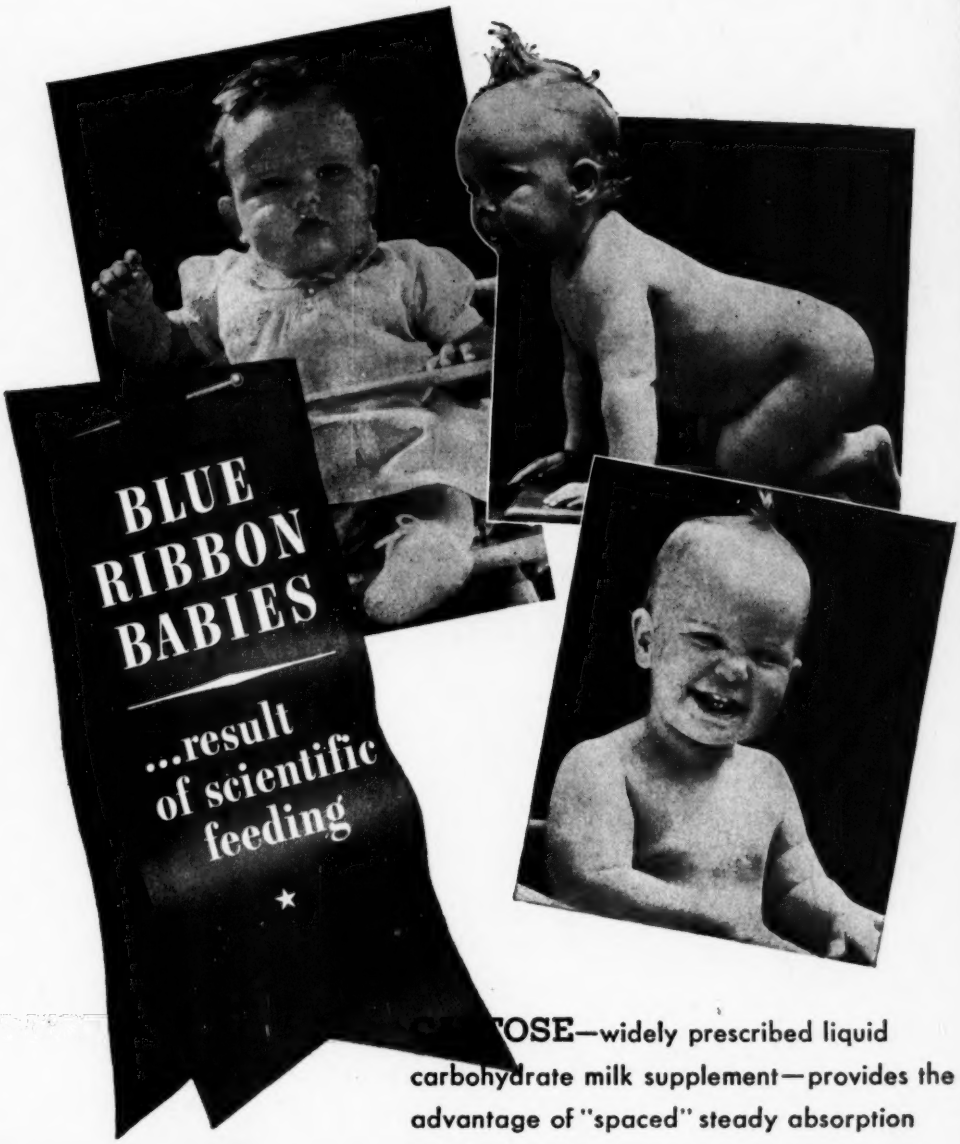

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